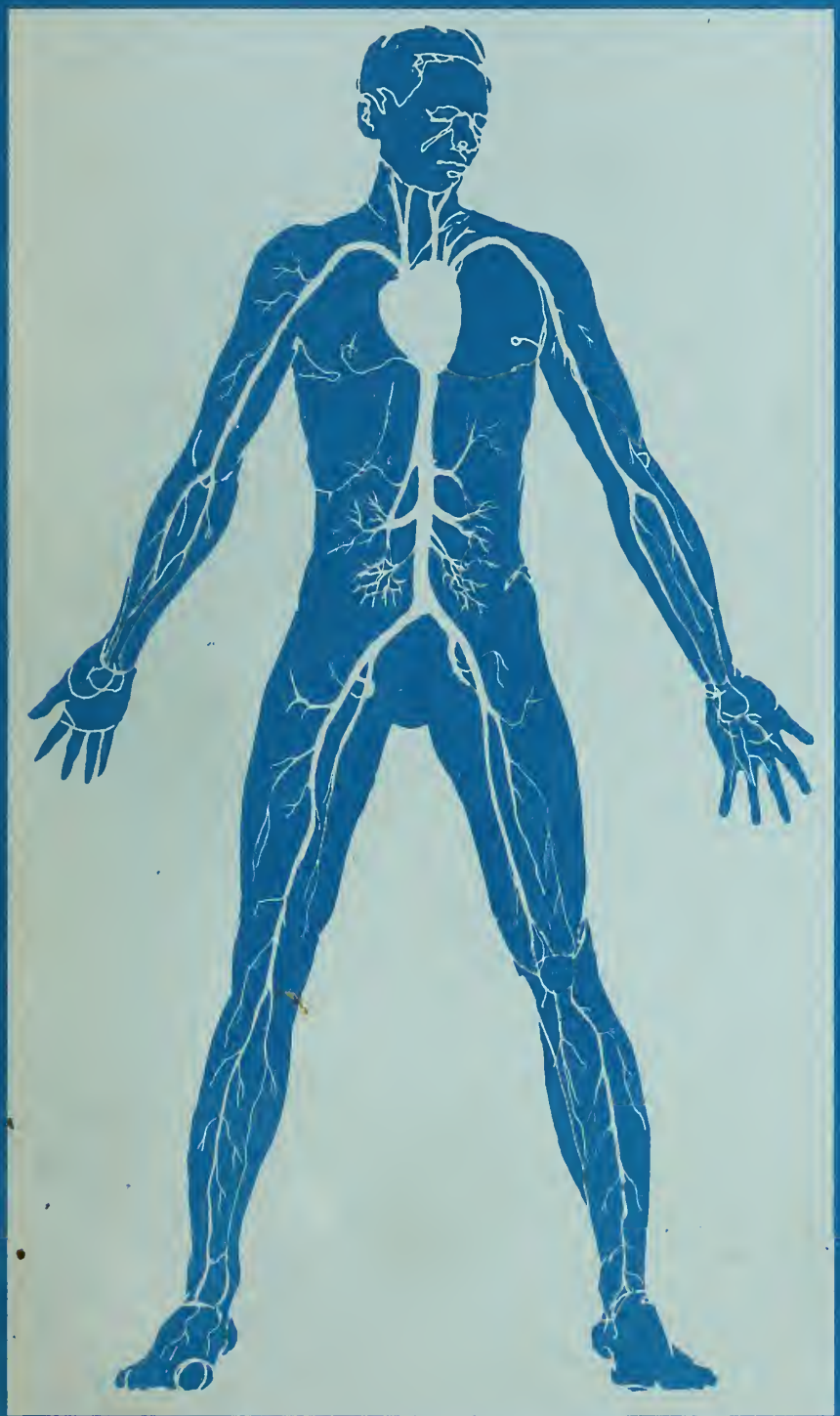
ARTERIOSCLEROSIS

REPORT BY NATIONAL HEART AND LUNG INSTITUTE TASK FORCE ON ARTERIOSCLEROSIS



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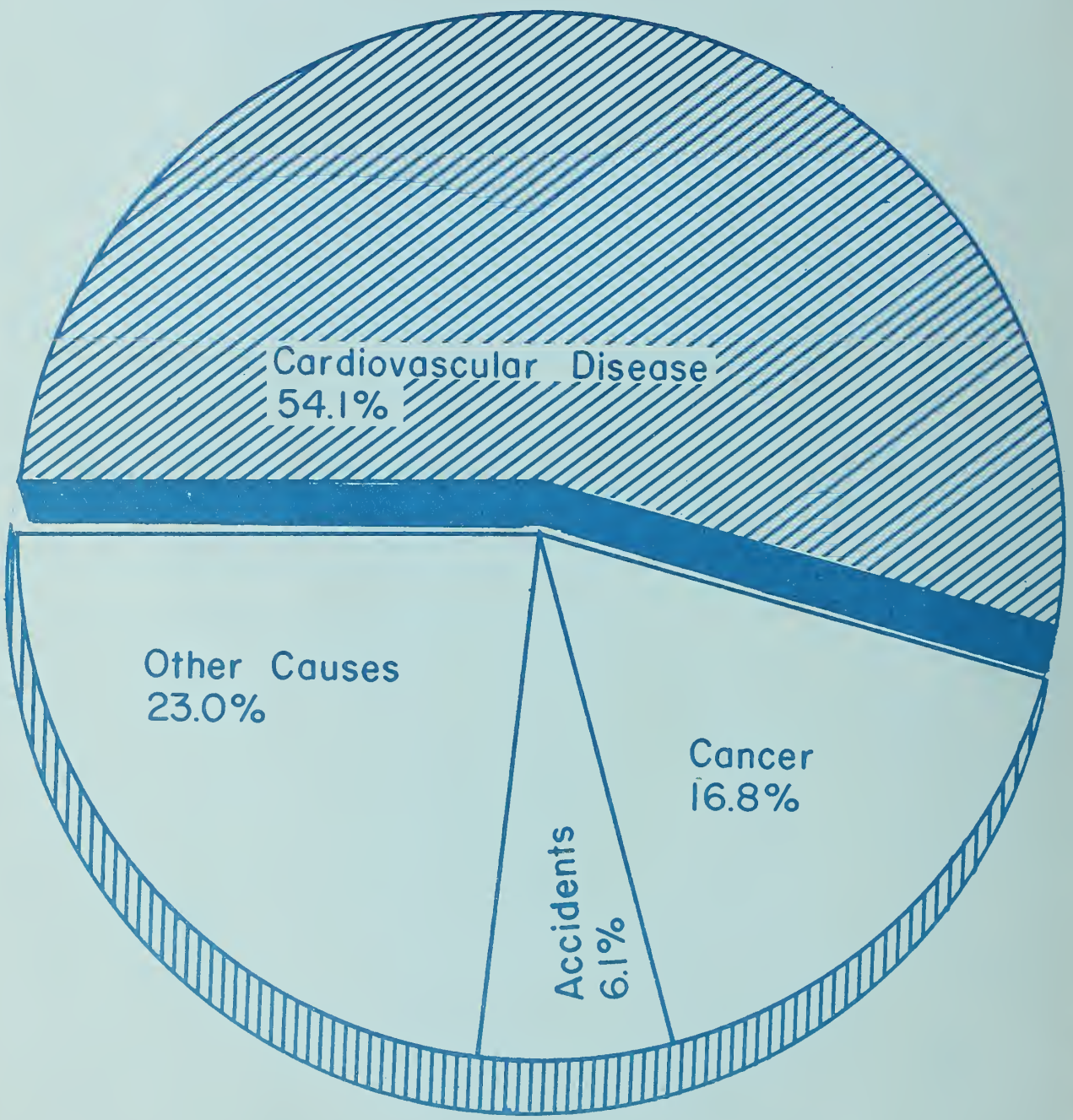

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ON
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NATIONAL
INSTITUTES
OF HEALTH

VOL. I June 1971

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"To him who devotes his life to science, nothing can give more happiness than increasing the number of discoveries, but his cup of joy is full when the results of his studies immediately find practical applications."

"There are not two sciences. There is only science and the application of science and these two activities are linked as the fruit is to the tree."

Louis Pasteur (1822–1895)

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I. INTRODUCTION

Arteriosclerosis* is the chief cause of death in the United States. Its victims, predominantly men, are frequently heads of households unexpectedly taken from their families at the prime of their productive lives. The cumulative personal and social losses are appalling.

Disappointingly, the United States ranks 24th in the world with respect to life expectancy for men. The high mortality from arteriosclerosis is one of the major contributing factors to this shortened life expectancy. The extent of the problem is exemplified by mortality from coronary heart disease, one of the major clinical manifestations of arteriosclerosis. In Denmark, Norway, and Sweden the mortality rate for men under the age of 55 is less than half that for the same age group in the United States. For Japanese men between the ages of 35 and 64, the death rate is 64 deaths per 100,000 population, compared to 400 deaths per 100,000 in the United States; a six-fold difference. Although attempts to learn why the United States fares so poorly in these comparisons have not been conclusive, studies have suggested that differences in diet, life-style, and personal habits may be important. Even more significantly, these studies have emphasized that arteriosclerosis is preventable and that certain influences called "risk factors" may be of particular etiologic importance.

Much thought and investigation already has been devoted to such risk factors as elevated blood lipid levels, hypertension, cigarette smoking and obesity. However, much more remains to be learned about the role of these factors and their interplay in the genesis of arteriosclerosis. Many authorities feel that proper application now of existing knowledge would decrease illness and death from arteriosclerosis. Indeed, a nationwide, coordinated effort to exploit our present understanding, to seek new knowledge, to remedy current inadequacies, and to establish new directions of inquiry seems timely.

Accordingly, Dr. Theodore Cooper, Director of the National Heart and Lung Institute, convened a Task Force on July 9, 1970 to develop a long-range plan to combat arteriosclerosis. The goal was a program aimed at prevention and control of the disorder, and effective treatment of its complications.

This report contains the results of one year of deliberations by the Task Force. The members met at regular monthly intervals to assess the magnitude of the problem of arteriosclerosis, to develop an understanding of its economic and social consequences, to evaluate currently available scientific information on the disease, to evolve conclusions and recommendations, and to formulate a long-range program for their implementation. The enormity of the problem necessitated the convening of panels of experts (see Appendix B) to assist the Task Force in carrying out its charge.

The report is published in two volumes of which this is the first. Volume I deals with general aspects of the problem and presents the major conclusions and recommendations. In order to communicate this information to interested and concerned individuals, who may be unfamiliar with medical terminology, an attempt has been made to present Volume I in nontechnical language. Volume II contains technical information on the current state of knowledge and conclusions and recommendations in each of the following areas: Atherogenesis, Presymptomatic Atherosclerosis, Overt Atherosclerosis, and Rehabilitation.

The report would not have been possible without the assistance of the individuals listed in appendix A, and the expert witnesses who made up the panels listed in appendix B.

*See Appendix C for glossary of scientific terms.

II. NATURE OF THE DISEASE

WHAT IS ARTERIOSCLEROSIS?

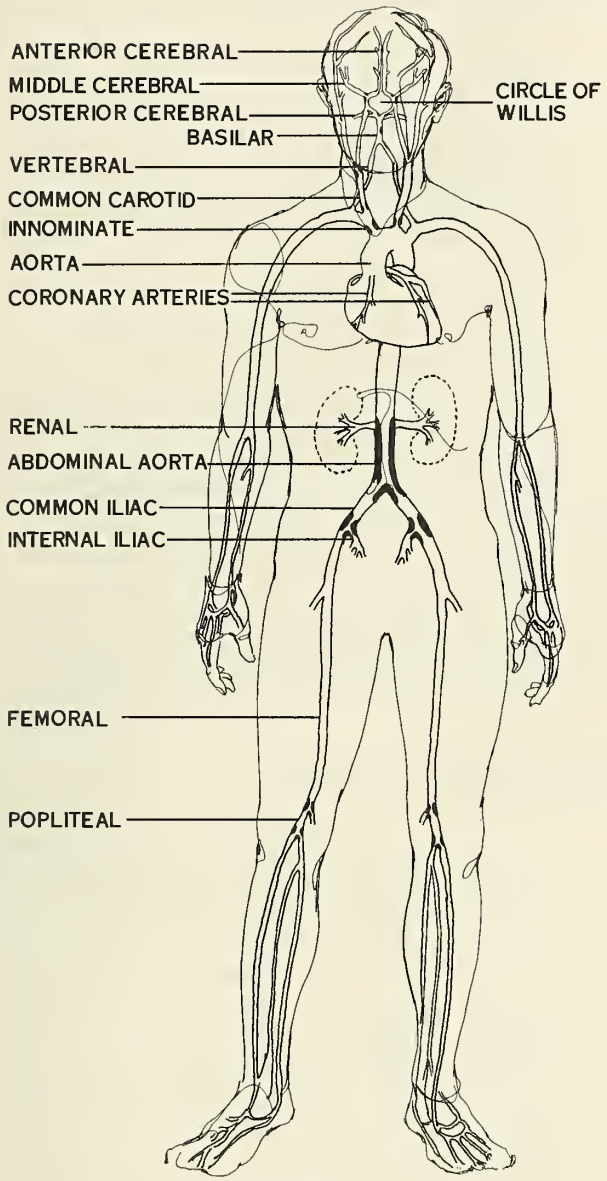

FIGURE 1
COMMON SITES OF ATHEROSCLEROTIC LESIONS

Arteriosclerosis literally means hardening of the arteries. In the type of arteriosclerosis responsible for the most important clinical complications, the inner layer of the artery is characteristically thickened by soft fatty deposits, called atheromas or atheromatous *plaques*. The blood vessel disease characterized by this type of deposit is often called *atherosclerosis* instead of arteriosclerosis. It affects both large and medium-sized arteries (Figure 1).

Atherosclerosis, which is the type of arteriosclerosis to be emphasized in this report, is generally a slow, progressive disease which may start in childhood. Its development may produce no symptoms for 20-40 years or longer. Even in advanced stages, it may be discovered only at post-mortem examination. It may be recognized during life by special X-ray examinations after injecting radio-opaque materials into the blood stream, thereby allowing visualization of the arteries. This technique is referred to as angiography or arteriography. In some cases atherosclerotic lesions containing deposits of calcium may be seen on routine X-ray examination.

THE ATHEROSCLEROTIC LESION

The basic lesion of atherosclerosis is the atheromatous plaque, which looks like a pearly grey mound of tissue on the inside of the blood vessel wall. It usually consists of a core of lipid (mainly cholesterol) covered by a cap of fibrous (scar) tissue. As these plaques increase in size, they may impede or cut off blood flow in affected arteries, causing damage to the tissues supplied by these arteries.

Our knowledge of the mechanisms by which plaques grow is limited. However, among the suspected mechanisms are: (1) thrombus (clot) formation on the surface of the plaque followed by fibrous organization of the thrombus, (2) hemorrhage into a plaque, and (3) continued lipid accumulation. In addition, the fibrous cap of a plaque may rupture and the lipid debris of the core be washed into the blood stream. This debris may cause obstruction of small arteries

and capillaries "downstream" from the ruptured plaque.

The mechanism by which plaques form in the wall of arteries is poorly understood. Many scientists believe that the plaque begins as a yellowish fatty streak. Fatty streaks are present in the aortas of nearly all children by age 3 years, and the streaks increase in number and size up to about age 25. Coronary artery fatty streaks usually begin to appear between ages 10 and 15, and increase in extent up to about age 25. Fatty streaks in the cerebral arteries do not usually appear until about age 35. Fatty streaks never are a cause of symptoms *per se*. Their sole importance lies in the possibility that they may develop into plaques. They are found in arteries of all populations that have been studied regardless of the incidence and prevalence of clinical atherosclerosis in older age. Except in the case of the coronary arteries, the extent of fatty streak involvement does not correlate with clinical disease later in life.

Considerable scientific information about the fatty streak has been developed from animal experiments. Fatty streaks can be produced in many animals by feeding a diet high in fat and cholesterol which raises blood lipid levels causing a condition called hyperlipidemia. Fatty streaks in humans and animals appear to be similar in cells and types of lipids present in the lesions. The cells are primarily smooth muscle, and the lipid is primarily cholesterol.

In animals, the induction of hyperlipidemia followed by appearance of fatty streak lesions provides experimental evidence supporting the hypothesis that elevated blood lipids tend to increase lipid deposition in arteries. The mechanisms by which lipids accumulate in fatty streaks are presently under intensive investigation, and their discovery undoubtedly will help to explain localization of lesions and reactions of the arterial wall to lipids.

One important problem is to determine if fatty streaks are transformed into plaques, and if so by what mechanisms. Although not all fatty streaks may evolve into plaques, the fact that some fatty streaks precede plaques and involve the same anatomical sites in the coronary arteries has led many investigators to conclude that fatty streaks are the precursors of plaques.

Atherosclerosis ultimately produces symptoms because the plaques cause marked narrowing or obstruction of affected arteries, thus diminishing or blocking blood flow to the organ or tissue supplied by the artery. Very severe or total occlusion may occur rather suddenly as a result of a blood clot developing on the plaque. This process of blood clot formation is termed *thrombosis*. When the affected organ or a part of it dies because of inadequate blood supply due to a blocked artery, the process is termed *infarction*. If an artery is partly, but not completely blocked by an atherosclerotic plaque, supplied organs may suffer from an inadequate blood supply called *ischemia* which is not severe enough to result in death of tissues. Occasionally the atherosclerotic changes may weaken the wall of the artery, causing a bulge, or *aneurysm*, which can rupture and cause hemorrhage into the tissues.

PRESYMPTOMATIC STAGE OF ATHEROSCLEROSIS

As indicated above, atherosclerosis begins early in life. It is probable that in the United States most men and many women beyond 50 years of age have moderately advanced coronary atherosclerosis, even though they are presymptomatic, i.e., have no symptoms of coronary artery disease. The absence of symptoms makes detection of the disease difficult; thus many of these individuals remain untreated.

There is now evidence that newer diagnostic procedures, including the recording of the electrocardiogram during and after exercise, greatly increase the ability of the physician to detect coronary atherosclerosis at the presymptomatic stage. However, such tests in their present form are neither highly sensitive nor specific. Moreover, they do not indicate the location or extent of the obstruction within the coronary circulation.

In recent years, the development of angiography has made it possible to depict the deformation, narrowing, or occlusion of the coronary arteries through special X-ray studies. As a means of following the natural evolution of the disease and the effect of therapeutic interventions, however, coronary angiography is not feasible as a routine diagnostic procedure in asymptomatic individuals because of the need for hospitalization, occasional serious complications, and practical difficulties associated with repeated examinations.

There is also a long presymptomatic stage of atherosclerosis involving the cerebral and peripheral arteries and the aorta. This stage is of particular importance in the case of the cerebral vessels since a patient's prospects are poor once cerebral atherosclerosis results in occlusion, and because some individuals can be

helped by prophylactic surgical procedures in the preclinical stage. Cerebral atherosclerosis may be detected by cerebral arteriography.

Atherosclerosis of the aorta may be recognized on conventional X-ray examination as elongation, tortuosity, dilatation, and sometimes by a large aneurysm of the artery. Frequently deposits of calcium are also recognizable. The most severe changes usually occur in the abdominal segment of the aorta where aneurysm formation can often be discovered by abdominal examination and by conventional X-ray examination long before symptoms occur.

CLINICAL MANIFESTATIONS OF ATHEROSCLEROSIS

The clinical symptoms and signs of atherosclerosis are due to narrowing or occlusion of an artery, resulting in inadequate blood supply to the affected organ; aneurysm formation; or rupture of the artery with hemorrhage into the surrounding tissues. The specific symptoms and signs depend on the organ or tissue affected.

1. *Coronary Atherosclerosis*

This is also termed arteriosclerotic or atherosclerotic heart disease or coronary heart disease. The major clinical manifestations are angina pectoris, acute myocardial infarction, sudden death, disturbances in rhythm and electrical activity of the heart, and congestive heart failure, all of which are described in the section which follows.

A. Angina Pectoris. When a coronary artery is sufficiently narrowed, the result is ischemia of the heart muscle, and the consequent symptom is chest pain or a discomfort in the chest termed "angina pectoris." This symptom usually occurs only intermittently with walking, other physical exertion or emotional stress, which temporarily increase the need of the heart muscle for blood beyond the available supply delivered by the affected coronary artery. As a rule, such pain subsides promptly with rest or drug therapy. Angina pectoris may occur with or without previous myocardial infarction (See next section).

The usual treatment of angina pectoris is designed to relieve the symptoms. It includes avoidance of activities which produce the discomfort, and the use of nitroglycerin. Physicians are not in agreement about the value of drugs with a longer action than nitroglycerin such as certain nitrates and other agents such as propranolol or anticoagulants. Other therapeutic recommendations include the attainment and maintenance of ideal weight, and the encouragement of moderate controlled exercise. There are ardent advocates of exercise programs and of coronary surgery for angina pectoris. The long-term value of these therapies has not been adequately assessed. Major handicaps in evaluating these forms of treatment include inability to predict the course of the disease in an individual patient, and difficulty in assessing progress or improvement in the underlying coronary atherosclerosis because of the practical problems in repeating coronary angiography or measuring coronary blood flow.

Angina pectoris usually persists for many years in a stable form, with brief, tolerable attacks. However, even at this stage, it is a serious disease. The affected patient may die suddenly, he may develop an acute coronary thrombosis with myocardial infarction, or the angina pectoris may become unstable. In the unstable stage, the episodes of chest pain become more frequent and more intense, occurring with less provocation or without any apparent cause, and responding less readily to rest and nitroglycerin. Such alteration in angina pectoris may be a warning signal of impending acute myocardial infarction.

B. Acute Myocardial Infarction. When the thrombotic occlusion occurs in one of the large coronary arteries that supply blood to the heart, the event is termed coronary thrombosis or coronary occlusion. Coronary thrombosis may result in death of heart muscle (myocardial infarction). Such infarctions are commonly termed "heart attacks." In common parlance the terms coronary thrombosis, myocardial infarction and heart attack are used synonymously, although they refer to different elements of the same total event. Typically there is warning pain or pressure in the chest occurring within hours or days before the actual infarction. This chest pain may be a new development or an increase in the severity and frequency of pre-existing angina pectoris.

The pain of acute infarction is similar to that of angina pectoris, but it is generally much more severe. It usually persists without interruption for at least an hour and is not relieved by nitroglycerin. At least half of the deaths from acute coronary attacks occur before patients reach the hospital. These early deaths may result chiefly from serious abnormalities in heart

rhythm, called arrhythmias, which may progress to the stage called cardiac arrest in which the heart stops functioning. Early detection and treatment of these arrhythmias may offer a great potential for saving lives. However, a significant percentage of these early deaths are extremely abrupt, with loss of consciousness and death within seconds or minutes. Such early victims could have been saved only by prevention of the basic disease (primary prevention), or by medication taken before the attack.

Treatment of acute myocardial infarction in coronary care units has reduced hospital mortality from about 30% to 20% or less, chiefly by preventing or controlling serious arrhythmias. More lives might be saved if such care could be instituted earlier, but most patients in an urban coronary care unit arrive more than three hours after their chest pain begins. The average delay is 7-8 hours. There is a clear need to educate both patients and physicians regarding the urgency for persons with symptoms of acute infarction to proceed at once to the nearest hospital or other appropriately equipped emergency medical facility. In addition, such facilities must be prepared to initiate treatment without delay.

Although the diagnosis of acute myocardial infarction occasionally seems equivocal, the great majority of patients can be diagnosed on the basis of the symptoms, electrocardiographic alterations, and the presence in the blood of increased amounts of certain enzymes derived from the damaged heart muscle.

The major complications of acute myocardial infarction are cardiogenic shock, congestive heart failure, and arrhythmias. During hospitalization, the major cause of mortality is cardiogenic shock which is fatal in 85% or more of cases. Because of extensive damage of heart muscle, the amount of blood pumped by the heart falls to two-thirds or less of normal, and there is a marked drop in systolic blood pressure (to 80 mmHg or less), causing inadequate blood flow to various organs of the body, notably the kidneys, which are unable to excrete an adequate amount of urine.

Available therapy for shock due to coronary occlusion is unsatisfactory. It consists of the use of drugs to increase the force of the heart beat, elevate the blood pressure, and promote urinary excretion. Recent developments in therapy include the use of various forms of mechanical cardiac assistance to aid the failing heart, surgical procedures aimed at increasing coronary blood flow, and the removal of infarcted and scarred tissue. Surgery also has been employed to repair certain complications of myocardial infarction, such as rupture of the interventricular septum, rupture of a papillary muscle, or a ventricular aneurysm. These new therapeutic approaches are still in the investigative phase. Further studies are needed to determine whether their widespread use would result in a marked prolongation of life in these patients.

The value of anticoagulant therapy in acute myocardial infarction is in its acknowledged reduction of thromboembolic complications.

Congestive heart failure is a serious complication of myocardial infarction which may develop during or after the attack. It may respond to medical treatment with digitalis, restricted salt intake in the diet and the use of diuretics.

Serious disturbances of heart rhythm may occur both during and after recovery from myocardial infarction. They are most frequent during the first few hours after the episode, and diminish in frequency thereafter. While certain of these are relatively benign, others are life-threatening and require immediate treatment, such as the use of electric shock to the chest wall, the use of various anti-arrhythmic drugs, and the use of such drugs in combination with insertion of a cardiac pacemaker. None of the available drugs is usually satisfactory for long-term use to control and prevent serious arrhythmias.

C. Sudden death. It has been reported that 50–65% of all sudden deaths are due to coronary heart disease. Conversely, fifty percent of all deaths from coronary heart disease occur suddenly and unexpectedly. Sudden death from cardiac disease has been defined as death occurring instantaneously or within an estimated 24 hours of the onset of acute symptoms or signs. The death is regarded as unexpected if the victim was not confined to home or hospital and at least superficially appeared to be able to conduct his usual activities. In several major studies, 50–65% of persons dying suddenly have had a previous history or symptoms of coronary heart disease. In one of these investigations, 25% of those who died suddenly had consulted a physician within the previous week.

Sudden death from coronary atherosclerosis may occur (1) in a patient with no previous symptoms; (2) in a patient with stable angina pectoris during or in the absence of an attack of chest pain; (3) in a patient with a history of myocardial infarction with or without angina pectoris; or (4) during an acute myocardial infarction, especially in the first hour or two after onset of the pain. The immediate mechanism of sudden death is believed to be ventricular fibrillation, (total incoordination of heart contraction) or less often, cardiac standstill. Sudden death may result from

ischemia without infarction if the result of the ischemia is a major disturbance of the rhythm of the heart.

The nature of the pathologic changes in the coronary arteries of individuals dying suddenly and unexpectedly is incompletely understood. The reported incidence of coronary artery thrombosis in such cases varies from about 20% to nearly 100%. A major cause for this large variation may be differences in the thoroughness or in the technique of examination for thrombi. Better understanding of the acute changes in coronary artery atherosclerotic lesions that cause sudden arterial occlusion could provide a basis for designing programs to prevent the condition.

In addition to a history of myocardial infarction or angina pectoris, other factors may be indicators of an increased risk of sudden death. These factors include certain recurrent disturbances in heart rhythm; electrocardiographic evidence of heart muscle damage, electrocardiographic abnormalities in response to stress tests; and the presence of certain risk factors including a history of smoking cigarettes.

2. Cerebrovascular Disease

Atherosclerosis of a given cerebral vessel causes no symptoms if the area of the brain supplied by the diseased artery receives adequate compensatory blood supply from other arteries (collateral circulation). Thus, in some cases, even severe narrowing or occlusion of an artery by atherosclerosis may produce no symptoms, especially if the process in the artery has been gradual. However, if blood flow to the brain falls below critical levels, or if the artery is sealed off by a clot or ruptures, symptoms of cerebral ischemia or hemorrhage will usually develop. The symptoms depend on the artery involved, the area of brain supplied, the nature of the collateral circulation, and the pathologic process in the artery (embolism, thrombosis, or rupture).

Because one area of the brain controls the muscles of the arm, another the leg, yet another the speech, and so on, disease of the blood vessel supplying a given area may result in symptoms such as paralysis of a limb or loss of speech. The degree and permanency of the disturbance determines whether the loss of function is partial or complete, and whether it is temporary or permanent.

A. Transient cerebral ischemic attacks. When there is a sudden, marked reduction in blood flow to the brain, there may be symptoms that are termed transient cerebral ischemic attacks. These are usually associated with partial obstruction of one or more of the brain's major arteries called the vertebral-basilar or the carotid arteries. Frequently, however, transient ischemic attacks are secondary to a number of factors such as the release of platelet thrombi or cholesterol from ulcerated plaques in the major arteries.

Obstructions to blood flow in the vertebral and basilar arteries which supply the brain stem may produce dizziness, loss of balance, ringing in the ears, double vision, speech disturbances, or difficulty in swallowing. Occasionally there may be weakness, numbness or tingling of an arm, leg, or the face, or temporary loss of vision.

Ischemic attacks due to obstructions of the internal carotid artery or its branches may cause transient weakness of the lower two-thirds of the face, fingers, hand, arm, or leg, and tingling or numbness of these areas. There may be transient loss of speech and understanding, and occasionally transient retinal ischemia resulting in temporary blindness.

These ischemic attacks indicate cerebrovascular disease. They serve as a warning of potential cerebral infarction, but whether and when such infarction will occur is unpredictable. About one-third of patients who eventually develop cerebral infarction suffer one or more transitory episodes of acute cerebral ischemia. If these are recognized and properly treated by appropriate drugs or surgical restoration of affected blood vessels, a major cerebral infarction may be prevented.

B. Stroke. Two general categories of cerebrovascular disease may result in symptoms which have been characterized as stroke, stroke syndrome, or apoplexy: (1) those secondary to narrowing or blockade of arteries resulting in ischemia or destruction of brain tissue (cerebral infarction) and (2) those resulting from rupture of arteries, causing brain hemorrhage. The former is associated primarily with atherosclerosis; the latter is associated with sustained hypertension with or without severe atherosclerosis.

While strokes may occur suddenly and without prior warning, many individuals at high risk of developing this condition can be identified prior to the event. Many occlusive and hemorrhagic strokes can be prevented by prompt treatment of the underlying cardiovascular disorder. As mentioned above, patients who develop occlusive stroke may experience premonitory symptoms signaling the impending stroke and may be saved from disability and death by appropriate drug therapy or modern blood vessel surgery. In the case of hemorrhagic stroke, the best way to identify the population prone to brain hemorrhage and to prevent

stroke is to measure arterial blood pressure and to treat hypertension, if present.

The course of the stroke depends on the degree, location, and duration of the damage. Intensive modern therapy and rehabilitation programs, if instituted early, can restore many stroke survivors to relatively active and productive lives. Although many patients recover completely, some are left with permanent paralysis of arm or leg, or with a speech defect. Many more lives could be saved and disabilities prevented if programs of prevention, modern therapy, and rehabilitation for stroke were made generally available to the many hundreds of thousands of Americans who annually develop this complication of cardiovascular disease.

3. *Atherosclerosis of the Aorta*

Atherosclerosis of the upper portion of the aorta (thoracic aorta) is relatively frequent, but is rarely significant clinically, whereas involvement of the lower portion (abdominal aorta) is particularly likely to produce symptomatic disease.

Aneurysm of the thoracic aorta due to atherosclerosis on occasion creates pressure on adjacent structures. This pressure may produce chest pain, breathlessness, hoarseness due to paralysis of a vocal cord, or signs of compression of the superior vena cava. The aneurysm may rupture and this may be fatal.

Abdominal aortic aneurysm is usually located just below the origin of the renal arteries. It can usually be felt on abdominal examination as an expansile, pulsating mass at the level of the umbilicus. Expansion of the aneurysm produces pain in the abdomen or in the lumbar or pelvic regions, and is a harbinger of leakage or impending rupture. Rupture is associated with pain and signs or hemorrhage, including shock. The seriousness of the aneurysm is not always directly related to its size. Small aneurysms may rupture, particularly if they are saccular (sac-like) in shape rather than fusiform (spindle-shaped). In general, if the aneurysm is small, therapy usually consists of conservative management including control of hypertension, if present. Surgical excision and replacement with a prosthetic graft are indicated for large or enlarging aneurysms, especially if associated with pain. Evidence of impending or actual rupture demands emergency surgery.

4. *Renovascular Occlusion*

Atherosclerotic occlusion of the renal arteries may cause atrophy of portions of the kidney and, if extensive, reduced kidney function. Partial occlusion of one or both renal arteries can be responsible for hypertension (renovascular hypertension). The blood-deprived kidney releases increased amounts of the enzyme renin. In the blood, this enzyme catalyzes the production of angiotensin, a substance which causes constriction of arteries resulting in hypertension. Hypertension of renovascular origin is suggested if there is a sudden onset of hypertension, acceleration of previously benign hypertension, onset before 30 or after 50 years of age, and absence of family history of high blood pressure.

5. *Peripheral Vascular Atherosclerosis*

Atherosclerotic occlusion at or near the bifurcation of the abdominal aorta into the two large arteries (iliac) to the legs causes severe cramps and pain in the buttocks and thighs with walking which are relieved by rest. These symptoms are termed intermittent claudication. If the symptoms are severe and disabling, the disease must be treated by surgery to replace or bypass the obstructed segment.

Atherosclerosis may also cause narrowing and occlusion of the arteries to the lower extremities. However, collateral circulation may suffice to prevent symptoms for prolonged periods of time. The symptoms and signs are those of intermittent claudication, but the pain is usually located below the knee. Precise determination of the nature, location, and extent of the occlusion requires arteriography.

Graded exercise, abstinence from smoking, and occasionally surgery are the usual recommended forms of treatment. Gangrene, or death of tissue may occur especially in cases associated with diabetes, and this often necessitates amputation of the limb.

6. *Pulmonary Atherosclerosis*

The arterial blood supply to the lungs differs from that of the periphery of the body in that the pressure in the pulmonary arteries is much lower and the blood contains less oxygen. Perhaps related to these factors, arteriosclerosis in the pulmonary arteries is less of a problem than in the rest of the arterial circulation. However, it may occur when blood pressure is high in the pulmonary arteries, whether due to disease of the left side of the heart or the lungs themselves, or in certain other poorly understood states.

When such increased pressure exists, there may also be disease of the smaller arteries of the lungs. Such processes are important clinically in relation to the basic heart or lung disease with which they are associated.

III. MAGNITUDE OF THE PROBLEM*

Three indices of the current extent of the arteriosclerosis problem in the United States are summarized below: (1) Mortality; (2) Morbidity; and (3) Economic Impact. Only the coronary and cerebral complications of atherosclerosis are included in this discussion.

1. *Mortality*

In 1967, diseases of the cardiovascular system were the underlying cause of approximately 1,000,000 deaths. This was about 54% of all deaths (Figure 2).[1] Although the cardiovascular diseases were more common among older persons more than one-third of all deaths among persons under age 65 were due to these diseases. In the age group 35 to 44 years, such diseases accounted for about 31% of all deaths. This percentage increased with advancing age. For example, about 70% of the deaths among persons aged 75 years and over were due to these diseases.

Arteriosclerosis and related diseases such as hypertension account for the major portion of deaths from cardiovascular diseases (Figure 3).[1] Virtually all arteriosclerotic and degenerative heart disease is due to atherosclerosis, as is most aortic and peripheral arterial disease. A large proportion of strokes is also due to hypertension and arteriosclerosis. Thus, almost 84% of cardiovascular mortality can be ascribed to arteriosclerosis and its complications.

*The magnitude of the problem is discussed in detail in the Appendix to Volume II of the report.

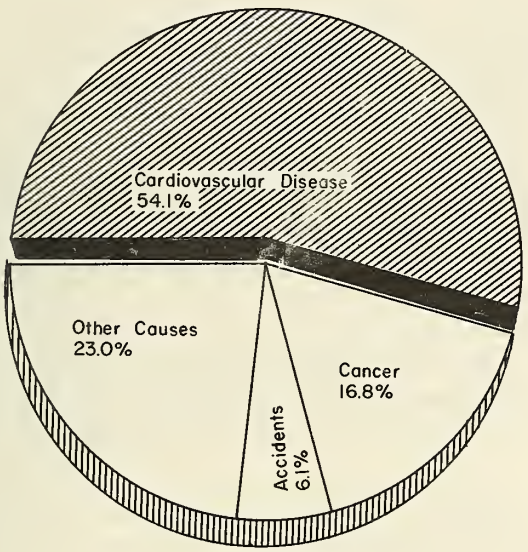

FIGURE 2

PERCENT DISTRIBUTION OF DEATHS FROM SPECIFIC CAUSES TO DEATHS FROM ALL CAUSES, UNITED STATES, 1967 [1]

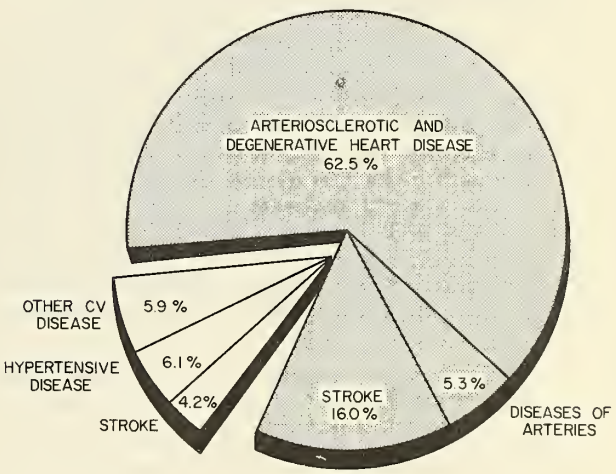

FIGURE 3

PERCENT BREAKDOWN OF DEATHS FROM CARDIOVASCULAR DISEASE BY MAJOR SUB-GROUP AND THE PROPORTION DUE TO ARTERIOSCLEROSIS (SHADED AREA): UNITED STATES, 1967 [1]

The approximately 626,000 deaths classified under *arteriosclerotic and degenerative heart disease* in 1967 (Figure 3) represented about 34% of deaths from all causes. The corresponding figure for persons 35 to 64 years of age was about 31%.

As indicated above, mortality from arteriosclerotic heart disease increases markedly with age. With the exception of the age group 75 years and over, the death rate in males is far greater than in females. This is especially true in younger age groups. For example, for the age group 45-54 years, the mortality rate in white males is 5 times that in females. In non-whites, the male-female differences are somewhat less pronounced.

Only Finland has higher death rates from all causes and from arteriosclerotic heart disease than does the United States (Figure 4).[2] The death rates from coronary heart disease (among men aged 45-54) in Sweden, Italy, and Switzerland are less than 40% of rates for similar groups in the United States.

The approximately 202,000 deaths in 1967 classified under *cerebrovascular disease* make it the third most common cause of death, after heart disease and cancer. The death rates increase markedly with advancing age, and, prior to age 75, are greater in the non-white population. All groups are experiencing a steady decline in death rates from this cause of death.

Elevated blood pressure is a major risk factor in arteriosclerosis. *Hypertension* is difficult to assess as a subgroup of mortality from the cardiovascular diseases. It is usually under-recorded as a cause of death, one of the reasons being that coronary disease or stroke tend to be listed as the underlying cause of death when either term is entered with hypertension on the death certificate. Nevertheless, in 1967, hypertension was listed as the underlying cause of about 61,000 deaths. However, we know that its role in death is considerably greater.

The non-white population has a much greater death rate from hypertension than does the white population, and as in the arteriosclerotic diseases, age is a very significant factor. The trend in death rates from hypertension has been downward in recent years.

2. *Morbidity*

(A) Prevalence. The number of cases of a given disease existing in a given population at a specified moment of time is referred to as the prevalence of the disease. Illness and disability from the clinical manifestations of arteriosclerosis are very prevalent in our population, and affect many individuals under 65 years of age.

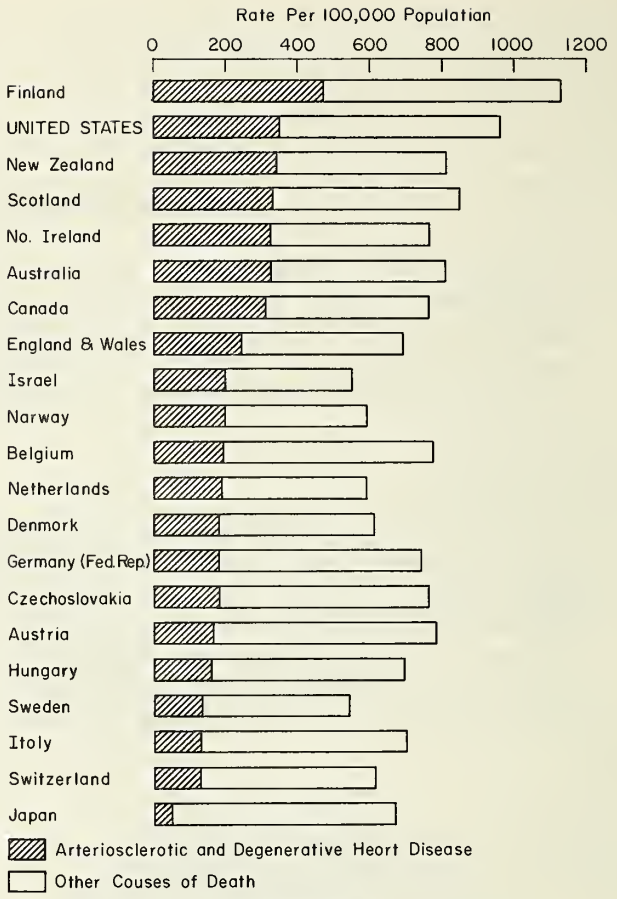

FIGURE 4

DEATH RATES FROM ARTERIOSCLEROTIC AND DEGENERATIVE HEART DISEASE AND FROM ALL CAUSES; SELECTED COUNTRIES, 1967—MEN AGED 45–54 YEARS [2]

The National Health Examination Survey of 1960-1962 showed that 5% of American adults aged 18-79 had definite or suspect coronary heart disease.[3]

The same survey also reported that 15% of this population had definite hypertension and another 15% had borderline hypertension.[4] The percent of young and middle-age persons with definite hypertension is significant; about 11% for persons 35-44 years of age, 18% for persons aged 45-54, and 27% for persons in the 55-64 age group.

The number of Americans who had had a stroke was almost 1.7 million in 1967; one-third were under 65 years of age. According to estimates from the National Health Interview Survey,[5] 1.5 million persons in the noninstitutionalized population had had a stroke.

Another 200,000 stroke victims were residents or patients of the nation's 17,400 nursing and personal care homes.[6]

(B) Incidence. A national study of incidence of arteriosclerotic events has not been conducted. However, estimates of incidence (the average number of new events of these diseases occurring in a one-year period), can be projected from one community population study, the Framingham (Massachusetts) study. These projections indicate that approximately 650,000 first heart attacks and 175,000 first strokes occur each year among Americans aged 35-74.

(C) Hospitalization. Of the approximately 28.8 million inpatients discharged in 1965 from the nation's 7,000 short-stay hospitals, 845,000 had arteriosclerotic heart disease as the diagnosis listed first on the summary sheet of the patient's hospital record. Stroke was the first-listed diagnosis for 370,000 inpatients, general arteriosclerosis for 104,000 inpatients, and hypertension for 288,000 inpatients.

3. *Economic Impact*

The "economic impact" or "economic cost" of a given disease represents the annual benefits that would accrue to the economy if that disease were eliminated or controlled. In 1967, the direct costs of illnesses from arteriosclerotic and hypertensive diseases amounted to $4.3 billion. Of this amount, $2.3 billion represents hospital costs (an estimated $1,100 per arteriosclerotic and hypertensive disease patient discharged), and $1.7 billion the cost of physicians' services, medication, and other personal care. Approximately 228 million man-years of work valued at approximately $1.1 billion were lost by members of the labor force and housewives due to illness from these diseases.

The indirect costs due to mortality, represented by the present value of the remaining lifetime earnings of the persons who died from these diseases in 1967, were estimated to be several times more than the direct costs.

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IV. RISK FACTORS AND PREVENTION

RISK FACTORS

Epidemiological studies have shown that coronary atherosclerotic heart disease occurs with increased frequency in association with certain characteristics present in the population under study or in their environment. These characteristics have been termed risk factors. The findings imply that the presence of one or more of these factors in an individual will increase the risk of arteriosclerosis and its complications and further, that removel or modification will diminish the risk. The likelihood of a causal relationship between the risk factors and the development of arteriosclerosis has led to the hypothesis that the incidence of this disease can be reduced by controlling or eliminating at least some risk factors.

The major risk factors indicated by numerous studies conducted chiefly in the past two decades are: (1) elevated serum lipids, specifically cholesterol and probably triglycerides, (2) hypertension, (3) cigarette smoking, and (4) elevated blood sugar (diabetes mellitus). Other risk factors for which there is some evidence include obesity, increased pulse rate, sedentary living, personality factors, certain patterns of behavior, and a family history of premature clinical atherosclerosis.

It is possible on the basis of these risk factors to identify persons especially susceptible to the development of the clinical complications of atherosclerosis and to develop programs of primary prevention, especially for children and young adults. Such preventive measures offer great promise of reducing the high mortality from complications of atherosclerosis. They may also be of value in reducing the threat of recurrent clinical episodes, i.e., secondary prevention, or postponing their onset. It is logical to decrease the intensity of the risk factors as early in life as they are detected and identified, since it appears that the development of arteriosclerosis is a life-long process.

1. *Dietary Intake of Lipids and Serum Cholesterol*

An association has been demonstrated between the amount and type of fat and the amount of cholesterol in the diet, the level of serum lipoproteins, and the development of atherosclerosis. Atherosclerosis was first experimentally produced by feeding diets containing cholesterol to rabbits; and diets containing large amounts of cholesterol and fats are now routinely employed to raise serum lipid levels and induce atherosclerosis in animals. In monkeys, the feeding of typical American (human) diets will produce the disease.

Epidemiological studies have demonstrated with few exceptions that populations consuming large quantities of saturated fat and cholesterol have a relatively high concentration of serum cholesterol and a high mortality from coronary heart disease. Conversely, the serum cholesterol levels and the mortality from coronary disease are low in populations with a low consumption of saturated fat and cholesterol. There appears to be a continuous relationship between coronary disease, coronary mortality and the concentration of serum cholesterol. For example, in the Framingham study, the incidence of coronary heart disease in men aged 45–54 with serum cholesterol levels of 220–249mg/100ml, which would generally be regarded as acceptable, was 48% higher than the incidence of this disease in the same age group with serum cholesterol levels under 220mg/100ml. Men with serum cholesterol levels of 250mg/100ml or higher had a greater than two-fold increase in risk of developing coronary heart disease than did men with cholesterols under 220mg/100ml.

It is important to stress that cholesterol levels of 220–249mg/100ml, which are often considered as satisfactory for the middle-aged American male, are higher than usually found among middle-aged males in countries with a low incidence of atherosclerosis. It may be that the optimal serum cholesterol level for the middle-aged American male is 200mg/100ml or less.

International mortality statistics in 1967 for 21 different countries show substantial differences in death rates from coronary disease. These differences have been positively correlated with differences in nutritional intake of total calories, saturated fats and cholesterol. The United States is the second highest on the list of mortality from coronary heart disease among

males age 45–54. The population of the United States is equally high in its relative intake of saturated fats and in its levels of serum cholesterol.

2. *Hypertension*

Elevated blood pressure is a major risk factor in arteriosclerosis and its complications. As with blood cholesterol, there is a progressive increase in coronary disease with increasing blood pressure even in the range generally regarded as normal. The susceptibility to arteriosclerosis of persons with hypertension is greater if their serum cholesterol level is also elevated. Conversely, in populations with widespread prevalence of hypertension but with a low level of serum lipids, the hypertension is not associated with a comparable increase in coronary heart disease. Hypertension is the major risk factor for strokes, whether due to cerebral thrombosis or to cerebral hemorrhage. The treatment of even moderate hypertension has been shown to result in a great reduction in the incidence of stroke.

3. *Cigarette Smoking*

There is a significant positive association between cigarette smoking and susceptibility to coronary heart disease. According to the 1964 Surgeon General's report on smoking, there is a 70% greater risk of dying from coronary heart disease among smokers than among non-smokers. The risk is especially high among those smoking two or more packs of cigarettes daily from an early age. Among heavy smokers who discontinue smoking, the risk decreases 25% in the first year, although it requires 10 years of non-smoking for the risk to return almost to that of non-smokers. Cigarette smoking seems to be the most important of the various risk factors for men who suffered a coronary attack before the age of 50. Smoking appears also to be associated with a disproportionately high incidence of sudden death. The risk of strokes also seems to be greater among smokers than non-smokers. In populations such as the Japanese who have a low incidence of coronary heart disease, cigarette smoking does not appear to have a significant influence on the disease, even in those with hypertension. It has been suggested that this lack of response to smoking might be related to a diet low in saturated fats and cholesterol or to a low incidence of atherosclerosis, but this issue needs to be resolved by further studies.

4. *Diabetes Mellitus and Impaired Glucose Tolerance*

Coronary heart disease occurs with greater frequency among diabetics than among non-diabetics, especially in younger age groups. Although the young and middle-aged female who is not diabetic is less susceptible to coronary disease than the male, this advantage is lost among females who are diabetic. Patients with known coronary heart disease have been found to have an increased incidence of abnormal glucose tolerance and elevated blood sugar levels.

5. *Family History and Genetic Factors*

There are some families in which premature and often fatal heart attacks occur with greater frequency than in others. It is uncertain to what extent this tendency is due to genetic factors, for example, disorders of fat or carbohydrate metabolism. The familial aspect might be due to the fact that families usually consume the same sort of diet, share the same modes of life, and thus have much more in common than their genes alone.

6. *Other Risk Factors*

According to insurance studies, obese persons have an increased risk of dying from clinical complications of atherosclerosis. In general, the relationship appears to apply to the extremely obese. The increased risk in obese individuals may be related to the higher incidence of hyperlipidemia, hypertension, and diabetes.

There are studies suggesting that the clinical complications of atherosclerosis, especially sudden death, are more common among those who have little physical exercise, but the reasons remain to be defined.

A number of other factors have been noted to increase the odds of developing atherosclerosis. The higher susceptibility of the male compared with the female has been mentioned, but the disparity diminishes somewhat when women pass the age of 60 years or when hypertension or diabetes is present. Additional factors which have been correlated with enhanced risk include emotional stress; electrocardiographic abnormalities; increased pulse rate; abnormal electrocardiogram in response to exercise; softness of drinking water; and elevated blood levels of uric acid. Risk factors may be strongly associated with a particular manifestation of arteriosclerosis and not with others.

7. *Combination of Risk Factors*

Two or more risk factors are commonly present in the same individual. Persons with three, four, or more definite risk factors form an especially high-risk group. The incidence of acute heart attacks in this high-risk group is far greater than in persons with no risk

factor or only one. Of 2,000 men between the ages of 30 and 59 followed in the Framingham study, 270 were regarded as being at relatively low risk because they had blood pressures less than 140/90, serum cholesterol less than 193mg/100ml. and normal electrocardiograms. The development of clinical heart disease in members of this favorable group over a 10-year period was only 1/7th of that which occurred in the total group of 2,000 men. Among men with slightly higher blood cholesterol (up to 250 mg/100ml) and slightly higher blood pressure (up to 160/95), both of which are often regarded as within normal limits, the incidence of clinical coronary heart disease was 4.5 times greater than in the low-risk group. Among men with still higher cholesterol and blood pressure levels, the incidence was 14 times as great, while in men whose electrocardiogram was also abnormal, the risk was 23 times as great. Such increase in risk for a disease so common in the American population constitutes a major challenge as well as an opportunity for correction by both the medical profession and a concerned public.

PREVENTION

It is clear to the Task Force that prevention, rather than treatment, of arteriosclerosis offers the greatest promise of reducing mortality. Once the clinical manifestations of arteriosclerosis are apparent, the consequences may be difficult, if not impossible, to correct. Since at least half of the patients who develop heart attacks die before receiving medical care, only primary prevention can affect a significant reduction in the number of sudden deaths. Moreover, a modestly effective program of primary prevention in asymptomatic subjects could readily accomplish the same overall effect on mortality as do the present hospital-based programs.

Three particular risk factors are amenable to modification and, presumably, to prevention of arteriosclerosis: hyperlipidemia, hypertension, and cigarette smoking.

Hyperlipidemia.

There are two general approaches to control of hyperlipidemia, diet and drugs.

a. Diet. Although there is some evidence to support the popular belief that blood lipids are casually related to arteriosclerosis, and that a decrease in total and saturated fats in the diet may help to prevent the complications of arteriosclerosis such as heart attack and stroke, this evidence is scientifically not entirely convincing. Therefore, recommendations concerning diet are based on personal impressions and fragmentary evidence rather than on scientific proof.

Intuitively, it would seem prudent to decrease the incidence of hyperlipidemia in the population of the United States by controlling diet. However, this would be a formidable venture if it were to involve changing the diet of the entire nation. Indeed, before advocating such a major revolution in diet, the Task Force concluded that convincing evidence should be sought that lowering the levels of lipids in blood reduces morbidity and mortality from arteriosclerosis.

A few modest beginnings along this line have already been made. In general, modifying the diet by substituting polyunsaturated for saturated fats has decreased morbidity and mortality. However, the effects of such modification have not been conclusively shown, either in normal individuals, or in persons at high risk of developing complications of arteriosclerosis.

In 1962, a group supported by the National Heart Institute* explored the feasibility of undertaking a long-term, nationwide prospective trial testing the hypothesis that coronary heart disease could be prevented by dietary measures in a large population specifically not at high risk. This National Heart Institute group, as well as a subsequent one, did advocate the undertaking of such a large scale, long-term prospective study. However, the current Task Force could not endorse this conclusion. The Task Force reviewed the evidence supplied by these two groups and heard testimony from experts concerning the practical aspects of such an enormous undertaking. In addition, information was gathered to actually prepare a specific protocol. On the basis of these extensive deliberations, the Task Force concluded that there is considerable uncertainty that a meaningful answer could be obtained or that the study could be carried through to completion.

The Task Force chose instead to recommend, for the present, more limited trials of diet, such as that which is currently being supported by the National Heart and Lung Institute in Minnesota, using a closed

*National Heart Institute became the National Heart and Lung Institute in 1969.

population. Such trials should be continued and expanded, and plans should be laid to organize and to implement a long-term prospective study if current trials and administrative arrangements indicate that such a trial is feasible. "Clinics" and "Centers" are being created which can act as focal points for the nationwide study (see below).

b. Drugs. An alternate or possibly supplementary way to handle hyperlipidemia is by the administration of certain drugs. Clinical trials using these drugs are currently underway. Particularly noteworthy is the coronary drug project which the National Heart and Lung Institute is conducting, involving approximately 8,000 men, 30 to 64 years of age who have suffered previous myocardial infarction. The drugs which are being administered under rigorous controls are estrogens, clofibrate, dextrothyroxine, and nicotinic acid. Enrollment of the population for this trial was completed in June 1969, and the clinical phase of the study is scheduled for completion in 1974.

Within the National Heart and Lung Institute Intramural Program, a study has been initiated of 250 patients with elevated levels of blood cholesterol. In these subjects, blood lipid levels will be correlated with the amount of atherosclerosis as determined by angiography. Half of the subjects will be treated using a combination of diet plus the cholesterol-lowering drug cholestyramine; the other half will receive only the diet. Coronary angiography will be repeated at two and five years. Every six months, cardiac performance will be evaluated in response to exercise.

Currently under development by the National Heart and Lung Institute is a third program which, at present, involves six cooperating groups called Lipid Research Clinics. These clinics will assemble a population of patients with hyperlipoproteinemia. At the outset, this program will obtain information on the prevalence of the different types of hyperlipoproteinemia at all ages ranging from infants to adulthood, and the manifestations of arteriosclerosis as a function of the type of hyperlipoproteinemia. In addition, the clinics will attempt to improve methods for detecting and classifying hyperlipoproteinemia. The Task Force urges that this program be expanded as expeditiously as possible to include clinical trials of treatment in order to determine whether correction of the blood-lipid abnormality by diets and drugs will modify morbidity and mortality from coronary heart disease. It is clear that expansion of the Lipid Research Clinics will also make it possible for them to conduct primary prevention trials in "high risk" patients and to act as focal points for more elaborate studies on larger populations.

Not only the Lipid Research Clinics but also the Special Centers of Research in Arteroisclerosis and Hypertension, and the National Centers for Prevention of Arteriosclerosis described elsewhere in this report will contribute subjects for primary prevention studies. Although these Centers will have other major missions, they also will afford opportunity for the large scale studies which were considered earlier in this section and were deemed impractical without organized mechanisms for handling large numbers of patients on special diets. By promoting a proper interplay among the different units that are being established by the National Heart and Lung Institute throughout the country, it would become possible to mount a nationwide effort to evaluate systematically the effects of drugs and diet and to carry such a venture through to completion using proper techniques and controls.

Finally, the Task Force believes the coordinated national effort should be related to the experiences that are being gained outside of the United States. For example, a primary trial of long-term treatment with clofibrate, a lipid-lowering drug, is now underway in Edinburgh, Prague, and Budapest under the aegis of the World Health Organization. In each city, 5,000 male volunteers, 30 to 59 years of age, are being recruited. Important data have already begun to be gathered. The Edinburgh study has shown that there are no important toxic effects of clofibrate, even though the treatment has been continued for 1-1½ years and appreciable reductions have been accomplished both in serum cholesterol (18%) and triglyceride levels (28%). The above-mentioned trials and other studies conducted in various parts of the world should be followed and critically evaluated. Active lines of communication should be established to promote free interchange and to avoid needless duplication among nations.

Hypertension.

This is the one risk factor in which adequately controlled clinical trials have shown that treatment is effective in decreasing the occurrence of some manifestations of arteriosclerosis, i.e., stroke and congestive heart failure. This was demonstrated in the Veterans Cooperative Study where it was shown that treatment of patients with mild as well as moderate hypertension resulted in a marked decrease in clinically evident cerebral vascular disease. Despite the impressive evidence that treatment is effective, numerous studies indicate that the treatment of hyper-

tension in the population is inadequate. For instance, in a county in Georgia, 70% of hypertensives were not receiving treatment at the time of the study. Of those found to be hypertensive, 41% did not even know that the condition was present. Only 47% of those receiving treatment had normal blood pressure readings; thus 53% of those taking medication were inadequately treated.

It is apparent that improvements in the health delivery system must and can be made in order to identify patients with hypertension and provide them with effective treatment.

A number of projects directed toward this goal are being supported by the National Heart and Lung Institute. One is a cooperative study of the treatment of mild hypertension, underway since 1966 in six Public Health Service Hospitals, in men and women between the ages of 21 and 55. This study should provide data as to the effectiveness of treatment in reducing cardiovascular illness due to hypertension.

Recently, the National Heart and Lung Institute initiated a program in nine communities throughout the United States to develop and evaluate methods of detecting and caring for hypertensive persons in the population at large. Initially, a population of about 3,000 hypertensives will be identified in their communities. Individuals will then be referred to various programs for medical care and periodic long-term follow-up. A major effort of the program will be the study of those patients who neglect taking adequate treatment. Procedures will be developed to improve participation both by helping to motivate the patients and by removing other barriers to compliance. Subsequently, the effects of treatment in terms of reduced death and disability will be studied in these patients.

Cigarette Smoking.

A number of studies have shown that individuals who stop smoking cgiarettes have a lower incidence of coronary heart disease than those who continue to smoke. In one study the death rate did not decline to that of non-smokers until 10 years after the cessation of smoking. The rate of decline appears to depend on the duration of smoking and number of cigarettes smoked. Thus far clinical trials have not been conducted in cigarette smokers to demonstrate that cessation of smoking reduces morbidity and mortality. A major controlled clinical study would involve keeping large numbers of individuals on a regimen of continuous high levels of smoking for an observation period of many years. Since there is impressive pathological, experimental, and clinical evidence linking cigarette smoking with disease not only of the cardiovascular system, but also of other organs including particularly the lungs, it appears that a major clinical trial would be both unwarranted and unethical.

V. MAJOR CONCLUSIONS AND RECOMMENDATIONS

GENERAL CONCLUSIONS

1. Death and disability from coronary artery disease (heart attacks), cerebral vascular disease (stroke), and peripheral vascular disease have reached epidemic proportions in the United States.

> These diseases are the major cause of disability in the United States and are responsible for approximately half of all deaths each year. Further, approximately 40 percent of all deaths during the productive years between ages 35 through 64 are due to these diseases. This rate of morbidity and mortality in the United States exceeds that in any other industrialized nation in the world, except Finland.

2. Approximately 80 percent of this death and disability occurs in individuals having one or more of three specific risk factors—elevated levels of blood lipids, high blood pressure, and cigarette smoking.

> A major national program of research and education must be undertaken in an effort to alleviate this epidemic by avoidance and/or correction of these risk factors.

3. The objective of the national effort must be the primary prevention of arteriosclerosis.

> Sudden death or irreversible damage to the brain or heart is often the first manifestation of arteriosclerosis. Persons who survive the acute attack are often left with impairments which may be exceedingly difficult to correct. Therefore, the most effective treatment is the prevention of the primary condition rather than the treatment of its complications.

4. The etiology and pathogenesis of the fundamental lesion remain to be elucidated. Therefore, an expanded bold and imaginative program of basic and applied research must be undertaken to identify causative factors.

> At this moment, efforts aimed at primary prevention of arteriosclerosis are not based on adequate information. A vigorous, integrated national effort of basic and applied research will provide the knowledge required for efficient prevention programs.

5. More effective application of existing knowledge will materially reduce disability and death from the complications of arteriosclerosis.

> Systems must be developed for the early identification of persons with arteriosclerosis or at high risk of developing the disease. Entry of persons suffering from acute heart attacks or stroke into the health care system must be facilitated, and specialized facilities for their subsequent care and rehabilitation must be expanded.

6. The federal role in the prevention and control of arteriosclerosis must be expanded to a degree commensurate with the magnitude of the problem if current intolerable human and economic loss is to be curtailed.

> The federal involvement is totally inadequate for the magnitude of arteriosclerosis on several accounts: sparse and discontinuous funding; a dearth of long-range planning; and uncoordinated programming. As a result, progress in reducing morbidity and mortality is destined to be erratic and inconsistent until provision is made for a coordinated national effort which has prevention and control as a long-term commitment of the highest priority.

GENERAL RECOMMENDATIONS

The Task Force recognizes that in any field of medicine one never has all the answers. It is aware that it would be discouraging and disillusioning to the public if it advocated sweeping measures which are not now feasible, or offered prescriptions which were of doubtful validity or acceptability. Of necessity, recommendations based on current knowledge may, in some instances, be tentative and further experiments may be needed to obtain firm data. It is not contradictory to offer the public the best current evidence and advice, so that the citizen may make intelligent and enlightened choices regarding his health, while at the same time proceeding as carefully and as rapidly as possible to strengthen and amplify the evidence by further research. After careful study of the problem of arteriosclerosis and its impact on the American people, the Task Force makes the following major recommendations:

1. A major health goal of the 1970's should be prevention and control of arteriosclerosis, as well as its fatal and disabling consequences. Leadership in fulfilling this national commitment should be assumed by the federal government.

2. To achieve this goal, the National Heart and Lung Institute should be directed to develop, promote, and support a national, coordinated, comprehensive program for the prevention and control of arteriosclerosis.

This program should include: (A) Acceleration of research at both the basic and applied levels: (B) Efficient application of the results of this research: (C) An effective health educational system designed to advise all concerned—the public, the medical and allied health professions, and private sector groups—about measures that are available for the control and prevention of arteriosclerosis and its complications.

3. The President should be requested to appoint a continuing national commission for the prevention and control of arteriosclerosis.

(A) The charge to this commission should be long-term planning for a coordinated effort directed at prevention and control of this disease.

(B) The commission should operate on a continuing basis in an advisory capacity to the Director, National Heart and Lung Institute. The composition of the commission should be patterned after that of the National Advisory Heart and Lung Council and include physicians, scientists, and interested citizens.

SPECIFIC RECOMMENDATIONS

1. National Resources

To implement this program in arteriosclerosis, current activities of the National Heart and Lung Institute must be augmented by the creation of new resources.

(A) National Centers for Prevention of Arteriosclerosis

The Task Force proposes the creation of centers unique in concept in that they will be concerned with all major facets of arteriosclerosis, including its prevention, epidemiology, genesis, clinical manifestations, and treatment. They should be located at several medical centers.

In 1971 there is in the U.S. not one categorical center for comprehensive study, prevention, and treatment of arteriosclerosis. Instead, the effort is fragmented into small programs at many universities and hospitals. These programs, excellent as many of them are, do not encompass a multidisciplinary attack on arteriosclerosis.

Some programs have concentrated on the study of serum lipoproteins, others have dealt with the arterial wall, thromboembolic phenomena, heart muscle, or with environmental factors (diet, stress, etc.). However, in none of the existing programs is there a sufficient number of cardiologists, surgeons, pathologists, physiologists, biochemists, and other professional personnel to establish an environment in which the par-

ticipants can interact in an efficient and meaningful manner. It is likely that progress in discovering the causes of arteriosclerosis has been slowed unnecessarily by the lack of categorical centers in which meaningful interaction between scientists and practitioners of medical specialties is a daily occurrence.

The various arteriosclerosis centers and Lipid Research Clinics now being promoted by the National Heart and Lung Institute will add greatly to ongoing research and screening in existing medical centers, but the scope of any one of them is insufficient to achieve the truly multidisciplinary approach that is essential for the solution of the problem of arteriosclerosis.

In order to accomplish their task in a reasonably efficient manner the National Centers for the Prevention of Arteriosclerosis must be many times larger than anything now designated as arteriosclerosis centers. They must be equipped with personnel and with instrumentation to deal with the study, detection, prevention, arrest and reversal of symptomatic and presymptomatic arteriosclerosis.

The arteriosclerosis prevention centers must actively engage in the screening of populations in order to identify persons of all ages who manifest the presence of risk factors or overt arteriosclerosis. These centers will provide an environment where new therapies can be promptly evaluated. Studies in the younger age groups should be initiated, and the effect of altering the psychosocial environment of these younger persons should be evaluated. For example, behavioral studies on smoking withdrawal, diet modifications or other health measures should be coupled with clinical evaluations of health status.

The categorical centers for the Prevention of Arteriosclerosis should be located on the campuses of major medical school-university complexes. The core staff should be appointed on the basis of excellence, field of specialization, and interest in participating in a unique undertaking directed toward the prevention of arteriosclerosis. Prevention and control of arteriosclerosis should be the major commitment of the professional staff in these centers. The staff should have university privileges and be given opportunity to participate in the training of students in medical schools and in other university departments.

Several mechanisms for the funding of these centers were discussed by the Task Force. One possibility would be funding of the construction of new facilities by the United States Government in the physical vicinity of the premises of a university or medical center. The facilities would be owned by the government but operated by the medical center under contract and staffed by the medical center with *long-term* support for the core operations being provided by government funds. Additional support for specific research projects or clinical trials could be obtained through the regular grant and contract mechanisms sponsored by federal agencies or by private sources.

The Task Force recommends that the Director of the National Heart and Lung Institute appoint a committee to investigate various organizational structures and mechanisms for long-term funding of these centers. This committee should consider the experience gained from previous long-term funding of mission-oriented research laboratories and centers, e.g. the Lawrence Radiation Laboratory and the Oak Ridge Natioanl Laboratory, and other similar centers in the United States. These centers should be evaluated in terms of degree of success, ability to attract top scientists, achievements, failures and strengths. The committee should make recommendations on how best to organize and fund Arteriosclerosis Prevention Centers which would have the strengths but not the shortcomings of previous centers.

(B) Cardiovascular Disease Prevention Clinics

Cardiovascular disease prevention clinics should be established within the framework of existing medical care, teaching and investigative programs. Initially five to ten such model units should be established.

The primary goals of these pilot screening clinics should be:

1. To serve as model or demonstration units of prevention in cardiovascular disease;
2. To develop highly efficient methods of detection of persons at increased risk of atherosclerosis and its complications;
3. To develop improved methods of intervention for each of the major risk factors;
4. To develop trained manpower skilled in the techniques of prevention in cardiovascular disease.

In order to fulfill their mission in preventive cardiology, these clinics should be appropriately staffed by clinicians, epidemiologists, behavioral scientists and allied health professionals. Methods of collection and handling of data should be standardized so that the information from the various clinics can be compared and coordinated. For this purpose a central coordinating mechanism should be created to set criteria, develop standardized methods, and evaluate results. The coor-

dinating center should be concerned with the dissemination of information generated by the clinics as well as with the training of personnel for other medical institutions.

(C) Office of Health Education

An Office of Health Education should be created within the National Heart and Lung Institute to serve as a clearinghouse for information concerning arteriosclerosis.

The role of this office should be to provide an effective program of education for the public, the medical and allied health professions, and private sector groups with respect to the prevention and control of atherosclerosis and its complications. Specific attention should be given to dissemination of available information regarding the importance of diet, hypertension, cigarette smoking, weight control, and other factors in the prevention of the disease; and to the importance of early detection and treatment of arteriosclerosis and its complications.

2. *Clinical Trials to Test the "Risk Factor" Hypothesis*

The Task Force recommends that clinical trials be conducted to examine the effects of modifying risk factors on the primary prevention of the complications of arteriosclerosis.

The likelihood is high that a causal relationship exists between risk factors and the development of arteriosclerosis, and that a reduction in risk factors will decrease the incidence of the clinical manifestations of arteriosclerosis. These probabilities have focused attention on the need to test the latter possibility.

The major risk factors have been identified by numerous studies, chiefly during the past two decades. These include: (1) elevated serum lipids (hyperlipidemia), specifically cholesterol and probably triglycerides; (2) hypertension; (3) cigarette smoking; and (4) diabetes mellitus. Other risk factors include a family history of premature clinical atherosclerosis, obesity, sedentary living, and probably certain patterns of behavior. However, the first three risk factors (hyperlipidemia, hypertension, and cigarette smoking) are generally regarded as most important.

(A) Hyperlipidemia. The high incidence of arteriosclerosis in the United States is associated with high levels of serum lipids in the population. However, there is as yet no conclusive evidence that reduction of these levels will decrease the morbidity or mortality from the complications of arteriosclerosis.

A definitive test of this hypothesis in the general population is needed. However, such a test presents formidable problems since it would require a large population young enough so that arteriosclerosis is still relatively limited, and one that would adhere to a standardized diet, or drugs, or both, for a period of approximately 7 to 10 years. Before embarking on such a massive undertaking, it would be desirable to carry out more modest clinical trials in target populations at high risk of arteriosclerosis. As described earlier in this report, several such trials are currently under way both in the United States and abroad. In addition, other trials should be initiated to supplement these on-going efforts.

(I) Expansion of "Lipid Research Clinics"

The National Heart and Lung Institute Lipid Research Clinics should be expanded in order to increase the population available for clinical trials.

Six clinics now exist at leading medical centers, and they are currently assembling a population of patients with hyperlipidemia. The immediate goals are described earlier in the report. These include clinical trials designed to determine effectiveness of diet and drugs in reducing mortality and morbidity. The Special Centers of Research in Arteriosclerosis and the National Centers for Prevention of Arteriosclerosis will provide another source of high risk patients for primary prevention studies. Conversely, the populations of the Lipid Research Clinics should be accessible to other National Heart and Lung Institute programs. This coordination should be, in large measure, a responsibility of the coordinating group described elsewhere in this report.

(II) National Diet-Heart Trial

A single large-scale national diet heart trial is not recommended. After lengthy deliberations the Task Force concluded that such a study is not feasible at the present time.

A number of clinical trials on the effects of modification of the diet have been performed. As discussed earlier in the section on Prevention, in 1962 the Na-

tional Heart Institute sponsored a study to determine the feasibility of undertaking a large-scale prospective study of the prevention of coronary heart disease by dietary measures.

The Task Force considered whether a single large-scale trial should be undertaken at this time. It reviewed a large body of scientific evidence pertaining to past experience with dietary manipulations and incidence of coronary heart disease. It heard testimony from many of the scientists currently most active in the field and reviewed the recommendations made to the National Heart Institute in 1968 by the Diet-Heart Review Panel. In addition, it held discussions with representatives from various governmental departments and from industry. The Task Force convened two panels of experts to consider technical aspects of a proposed protocol.

The Task Force discussed at length the advisability of recommending to the National Heart and Lung Institute the support of a single large, long-term study to attempt to obtain evidence that through alteration of the fat content of the diet of the general population of the United States there could be attained a reduction in mortality and morbidity from arteriosclerosis and its complications.

Upon review of all this evidence, the majority of the Task Force members felt it unwise to mount a single, major, national diet-heart trial in the general population of the United States at this time. This conclusion was based mainly on three convictions: that one might well fail to obtain the desired definitive scientific answer from this huge undertaking; that the managerial problems of carrying out a well-controlled study with such a large free living population (estimates ranging from 24,000 to 115,000 individuals) in a country where an average of 18 percent of the total population move annually, and for the lengthy period of time (7-10 years) required to obtain a sufficient number of clinical events in the study population would make the study difficult to complete; finally, in view of these uncertainties, the projections of manpower and dollar costs (ranging from $500 million to more than one billion dollars) for such a study are formidable.

The Task Force expressed serious reservations about several of the fundamental assumptions upon which the experimental design of the proposed trial was based. These included the assumptions relative to the specific reduction in serum lipids which could be achieved in a free living population, and the magnitude of the reduction in the number of arteriosclerotic events which would constitute the endpoints of the study. The Task Force was also concerned about the inevitable high dropout rate when individuals are required to adhere to rigorous dietary prescriptions for many years. Also, as the national diet undergoes subtle but important changes over a period of years, the control subjects might approach the experimental group in dietary habits, thus interfering with the evaluation of the basic hypothesis. In addition, the Task Force concluded that subjects adhering to a diet regimen would most likely modify other risk factors. This would negate some of the basic assumptions of the study and make it difficult to interpret the results. Finally, the Task Force was concerned over the loss of satisfactory control subjects over a period of years as other risk factors such as smoking habits and hypertension are affected by other national programs.

As discussed earlier in this report, the Task Force feels that a definitive test of the lipid hypothesis in the general population is urgently needed. However, in view of the great uncertainty as to the feasibility of completing a single, large long-term study and obtaining a meaningful answer, and in view of the estimated costs in relation to this uncertainty, the Task Force does not recommend that such a single, major national study in the general population be supported by the National Heart and Lung Institute at this time. The Task Force does recommend that before considering such a major undertaking, the National Heart and Lung Institute continue with smaller, well-controlled studies, described elsewhere in this report, to determine whether lowering of blood lipids by diet or drugs will result in decreased incidence of clinical disease.

(B) Hypertension. Clinical trials have demonstrated that successful treatment of hypertension decreases the incidence of some of the complications of arteriosclerosis, particularly stroke. Clinicians are agreed that blood pressure should be lowered in patients with unequivocal hypertension. But the degree of elevation and the level of blood pressure requiring therapeutic intervention remain unclear. Moreover, although many effective therapeutic agents are available, several have side effects which make their continued use for long periods of time in patients exceedingly difficult. Consequently, the Task Force recommends studies:

1. **To define, in both sexes and at various ages, the levels of blood pressure that enhance the risk of developing the complications of arteriosclerosis;**
2. **To establish the long term effects of therapeutic agents, and**

3. **To develop means of encouraging adherence to long term therapy, particularly in asymptomatic individuals.**

A number of projects directed toward these goals are currently being supported by the National Heart and Lung Institute. These include a cooperative study of the treatment of hypertension that has been in progress since 1966 in six Public Health Service hospitals. Also, the Institute recently awarded five grants for Specialized Centers of Research in Hypertension. In addition, the National Heart and Lung Institute has initiated a program in which clinics will be established in nine communities throughout the United States in order to detect patients with hypertension and to develop methods by which adequate and continued long-term treatment can be accomplished. These studies should be continued and expanded in order to generate an adequate population in which treatment of hypertension can be effected under controlled conditions.

(C) Cigarette Smoking. Smoking is importantly related to arteriosclerosis and its complications. A variety of investigations have established an association between cigarette smoking and heart attacks. There is evidence that cessation of smoking decreases the likelihood of death and disability from heart and blood vessel disease. The current evidence indicates that the effects of cigarette smoking may be increased in the presence of other risk factors, such as hyperlipidemia.

The Task Force believes the evidence relating smoking and vascular disease is convincing. It recommends that the National Heart and Lung Institute assume responsibility for:

1. **An expanded program of advice to the public regarding the relationship between smoking and heart disease;**
2. **Support for behavioral research aimed at developing more effective methods of cessation of smoking;**
3. **Development of effective programs for the prevention of smoking, particularly in the young; and**
4. **Research into the basic mechanism by which cigarette smoking exerts its harmful effects.**

Cessation of smoking should be one of the major interventions of the multifactor trial recommended by the Task Force as discussed under the next recommendation.

(D) Multifactor Prevention Trials. In addition to clinical trials in which treatment is directed toward a single risk factor, trials can be undertaken where treatment is directed simultaneously toward a number of risk factors. Such combined intervention more closely resembles the type of intervention that would be carried out by a physician in his treatment of a patient.

The Task Force recommends that the National Heart and Lung Institute undertake multiple risk factor intervention trials in individuals at high risk because of combinations of elevated serum lipids, hypertension, and cigarette smoking. These trials will have the merit of demonstrating whether or not intervention can prevent the complications of human arteriosclerosis since this is the crucial question as yet unanswered by direct experiment. These trials would not delineate the effects of the various individual risk factors.

The Task Force reviewed this question and convened a panel of experts to consider such trials. It was concluded that such trials would be feasible. These trials would require populations of manageable size and would be likely to yield a meaningful answer. Similar studies are also in various stages of planning or in operation in European countries under the auspices of the World Health Organization.

(E) Exercise. Exercise can be recommended to increase stamina, promote a sense of well-being, aid in muscular development, reduce pulse rate, and in general, increase (in persons so disposed) the quality of life. There is evidence, thus far incomplete and inconclusive, that regular exercise may decrease either the rate of development of arteriosclerosis or of its consequences. But there are definite hazards associated with irregular and unsupervised exercise in the middle-aged and elderly.

The Task Force recommends that research relative to the role of exercise be continued and accelerated. However, the Task Force concludes that there is insufficient evidence at this time for advocating a major national effort aimed at increasing the level of physical activity for the purpose of preventing or modifying coronary arteriosclerosis. Also, the Task Force recommends that information concerning the hazards of unsupervised abrupt changes in physical

activity in middle-aged and elderly persons should accompany any advice that is given with respect to exercise programs.

(F) Antithrombotic agents. Practice varies with respect to the use of antithrombotic agents in occlusive disease associated with arteriosclerosis. In part, this discrepancy in practice stems from inconclusive evidence concerning the efficacy of such agents in the prevention and treatment of occlusive arterial disease. In addition, each agent poses problems in long-term use.

At the present time, there are several drugs that are potentially useful as antithrombotic and thrombolytic agents. In addition, several agents are currently under development and clinical trial. For example, streptokinase is being tested for its efficacy in myocardial infarction, and trials with urokinase are in prospect.

The Task Force recommends that attempts be continued to develop safe and effective antithrombotic agents and that they be assessed for their value in preventing or alleviating the complications of arteriosclerosis.

(G) Arteriosclerosis in the young population. In recent years, it has been recognized that abnormal lipid patterns predisposing to arteriosclerosis can be detected in early life. In addition, it is also appreciated that habits of activity and eating acquired in childhood set the pattern for later life.

The Task Force recommends a new concentration of effort to alert physicians concerning risk factors as they appear in childhood and young adulthood. A nationwide program of education should be developed to inculcate desirable habits of eating and physical activity. Motivational psychologists may be helpful in formulating suitable programs for encouraging the avoidance of smoking and overweight.

(H) Statement to the public on risk factors. The Task Force endorses the following statement to the public with regard to risk factors:

Epidemiological and laboratory studies have uncovered several factors which are associated with an increased risk of developing atherosclerotic heart disease and other manifestations of arteriosclerosis. Elevated serum lipids, high blood pressure, and cigarette smoking are major controllable risk factors.

It is not known whether all risk factors are causally related to atherosclerotic cardiovascular diseases, but the best judgment from present knowledge indicates that a significant reduction in the incidence of such diseases may be achieved by observing the following guidelines:

Blood Lipids **(cholesterol and triglycerides): Elevation of serum lipids is implicated in the etiology of arteriosclerotic disease. Current data indicate that the average North American has higher than optimal blood lipid levels and ingests excessive calories, saturated fat and cholesterol. Pending confirmation by appropriate diet or drug trials, it therefore would appear prudent for the American people to follow a diet aimed at lowering serum lipid concentrations. For most individuals, this can be achieved by lowering intake of calories, cholesterol, and saturated fats. An attempt should be made to attain and maintain optimal weight through weight loss by balancing caloric intake and energy expenditure. In certain individuals with clearly elevated levels of serum cholesterol or triglycerides, close medical supervision with more vigorous attention to the diet and the use of drugs may be necessary.**

High Blood Pressure: **There is conclusive evidence that control of elevated blood pressure by appropriate drugs decreases the occurrence of important complications of arteriosclerotic disease. Treatment of hypertension should be early, carefully regulated, and sustained under medical supervision.**

Cigarette Smoking: **Since cigarette smoking has been demonstrated to be an important risk factor in arteriosclerotic disease, all smokers should be urged to stop. Young people should be vigorously deterred from starting to smoke.**

3. Reducing Death and Disability

Noninvasive diagnostic techniques are urgently needed to enable the earlier identification of the individual with presymptomatic atherosclerotic disease.

Currently, the physician is severely limited in the means at his disposal to detect the existence and magnitude of coronary, cerebral, or peripheral arterial disease. The availability of more sensitive techniques for measuring the severity of preclinical atherosclerosis would greatly improve the identification of persons in whom early treatment is most needed as well as provide more accurate methods for monitoring the progress of this insidious disease.

Coronary artery disease

(A) Prevention of sudden coronary death. One-half or more of the deaths from coronary heart disease occur suddenly. Currently, there is no concerted, effective approach to reducing the truly enormous magnitude of this problem.

> **Therefore, the Task Force recommends a broad and vigorous program by the National Heart and Lung Institute to: (1) educate the public and especially high risk persons regarding the nature of significant symptoms of impending heart attack; (2) educate the public so that persons having significant symptoms will proceed directly to an emergency station; (3) develop standards of emergency medical care for persons with significant cardiovascular symptoms; (4) increase the availability of emergency facilities in all communities; and (5) develop improved pharmacologic and other approaches to prevention of life-threatening arrhythmias.**

(B) Angina pectoris. Millions of Americans suffer from angina pectoris. Although much remains to be learned concerning its mechanisms, the fundamental defect is a lack of adequate oxygen delivery to the heart. Current treatment is dominated by the use of drugs which are directed to reduce the disproportion between the oxygen supply to and requirement for oxygen by the heart. In recent years, surgical approaches to this disorder have been advocated as a more effective measure not only for alleviating symptoms but also to partially remove the threat of myocardial infarction and sudden death. However, there is as yet no adequate evaluation of the relative merits of the surgical versus the non-surgical forms of therapy.

> **The Task Force recommends that a concerted effort be made to obtain a reliable evaluation of surgical procedures being performed to revascularize the heart.**

(C) Minimizing mortality and complications of myocardial infarction. Ample evidence indicates that the mortality rate from myocardial infarction can be substantially reduced by prompt and specialized care. Such care is currently available in approximately 2,500 hospitals in the United States. This specialized care involving continuous electrocardiographic monitoring and early intervention in life-threatening arrhythmias need not be restricted to rigidly circumscribed hospital areas, i.e., "coronary care units."

> **The Task Force recommends that the National Heart and Lung Institute support projects for the demonstration of the coronary care concept for the management of arrhythmias complicating myocardial infarction. This undertaking should include the development of effective systems for electrocardiographic monitoring that are particularly applicable to widespread use. Present constraints in Federal Communications Commission regulations should be modified to enable radiotelemetry to central monitoring stations manned by personnel specially trained in the recognition and treatment of cardiac arrhythmias.**

Despite the recent advances in the management of cardiac arrhythmias, mortality from non-arrhythmic causes remains extremely high, about 20% in coronary care units. This mortality rate is primarily attributable to cardiogenic shock and congestive heart failure.

> **The Task Force recommends that the National Heart and Lung Institute continue to support intensive research into the mechanisms responsible for these complications of myocardial infarction and for their effective treatment. In addition, new modes of therapy require further development and critical evaluation. These include devices to assist the failing circulation and surgery to bypass the obstructed artery.**

(D) Rehabilitation of the patient after Myocardial Infarction.

At present, there is no systematic approach to the rehabilitation of the patient after myocardial infarction either from a psychological or physical point of view. Medical and nursing curricula generally contain little on this aspect of myocardial infarction and often provide inadequate information concerning available techniques and community services.

The Task Force recommends that the National Heart and Lung Institute assess the need for a more vigorous and direct approach to the rehabilitation of the patient after myocardial infarction. The medical as well as allied aspects of this problem should be evaluated, and attempts made to stimulate research in this area.

Cerebrovascular Disease

In the United States, arteriosclerosis is the predominant cause of stroke. Hypertension has been identified as the single most important risk factor for stroke. Occlusive cerebrovascular disease may be manifest clinically as brief episodes of inadequate cerebral blood flow (transient ischemic attacks) or as a stroke. Approximately one-third of patients with such transient attacks will subsequently develop stroke.

Current care of stroke patients is inadequate on several accounts. Many institutions are ill-equipped in terms of professional staff and facilities to cope with stroke. Current stroke centers are concerned with investigational aspects rather than with therapy and rehabilitation.

The Task Force recommendations on hypertension are described earlier in this report. In addition, the Task Force urges a wider appreciation of transient ischemic attacks as a warning of impending stroke in order to institute adequate treatment promptly. For these purposes, a program of education will be required to heighten public and professional awareness of warning signs and symptoms of inadequate cerebral blood flow and brain damage.

The Task Force recommends the creation of special care units to develop and demonstrate methods for optimal treatment of patients with stroke and for training personnel in these methods. The prompt application of modern techniques of rehabilitation should be included as part of these programs.

Peripheral Vascular Disease

There are millions of patients with peripheral vascular disease in the United States. In many, the process has been accelerated by diabetes mellitus. Many patients suffer needless disability because the disease is not recognized and, therefore, treatment is not initiated until it has become too far advanced.

The Task Force recommends an increased awareness by physicians of peripheral vascular disease, including that it may be prevented by attention to the risk factors previously discussed. There is a serious need for developing simple methods of diagnosing vascular insufficiency as well as a need for intensive medical care in order to avoid irreparable complications. In this field there is considerable need for allied professional personnel such as podiatrists and technicians for assisting with diagnostic measures and treatment. The Task Force recommends that the National Heart and Lung Institute take inventory of this field in order to assess the status of current knowledge and medical practice.

Socio-Economic Rehabilitation

The Task Force recommends that the institute initiate a study of the Socio-Economic rehabilitation problems of cardiovascular patients.

It has been estimated that one-half of our physicians are ill-informed or uninformed as to available socio-economic rehabilitation services.

The Task Force recommends that the National Heart and Lung institute, in conjunction with other governmental agencies, consider ways in which patients suffering from cardiovascular disability who receive financial support for an extended period of time from governmental or non-governmental sources may be automatically offered an opportunity of referral for rehabilitation.

The present application of Workmen's Compensation to patients with arteriosclerotic disease and its complications is frequently not based on solid scientific evidence, and has resulted in unjustified barriers to the employment of many persons with a history or signs of cardiovascular disease.

Therefore, the Task Force recommends that the National Heart and Lung Institute, in conjunction with other government agencies and representatives of the legal profession, consider ways in which persons disabled by arteriosclerotic disease in the course of employment might best be covered by comprehensive insurance in order to obviate the delays, litigation, and ambiguities incident to the application of workmen's compensation.

4. *Recommendations for Research*

(I) The cure of a disease is generally found in the discovery of its cause. There are still major unanswered questions about the cause (or causes) of atherosclerosis. Involved in the answer to these questions are blood lipids and lipoproteins and the factors determining their levels, the arterial wall and its role in the production of fatty streaks and plaques, and clotting mechanisms and their role in thrombosis. In addition, the mechanisms whereby genetics, hypertension, cigarette smoking, diabetes, physical exercise, and behavior exert their effects are not fully known. Therefore, in addition to the many research projects recommended above, the Task Force emphatically recommends the strong support of basic research in atherosclerosis and in other aspects of the biological sciences since important discoveries related to atherosclerosis might well be made in fields outside cardiovascular research.

(II) It is recommended that the National Heart and Lung Institute establish a system of international exchange of information on current activities in arteriosclerosis, in order to accelerate progress and promote solutions within the next decade. It may be necessary in certain instances to consider collaborative research programs with other countries as well as exchange of information.

5. *Manpower Development and Training*

A bold and vigorous program has been presented to understand, prevent, and treat arteriosclerosis and its complications. In order to implement this program and assure success in future years, the Task Force recommends an intensive effort by the National Heart and Lung Institute to stimulate training programs and manpower development in those areas vitally concerned with cardiovascular diseases.

In addition to the clinician in both the medical and surgical specialities, the National Heart and Lung Institute must promote manpower development in other areas where there presently are shortages. These efforts should include programs to train epidemiologists, biostatisticians, and scientists interested in the psychological and behavioral aspects of arteriosclerosis. The National Heart and Lung Institute should set up effective training programs in these and other areas of manpower needs and recruit individuals of diverse backgrounds for this training.

Programs that have been initiated by the National Institutes of Health during the past decades have resulted in the development of a unique pool of individuals trained in such areas as biochemistry, physiology, pathology, and pharmacology, and their applications to clinical problems. The development of knowledge necessary for the prevention and treatment of atherosclerosis will depend on the continuous entry of these individuals into the field.

The basic sciences such as biochemistry, endocrinology, physiology, pathology, and pharmacology must be encouraged to produce more and better equipped physicians and scientists trained in arteriosclerosis research.

6. *Managerial Aspects of Atherosclerosis*

Historically, much of the success of preventive medicine has been achieved by affecting the environment.

To the extent that the food industry can influence the composition of the American diet including its content of saturated fats, cholesterol and salt, and the tobacco industry can control the nicotine and carbon monoxide contents of tobacco smoke, these industries should be given incentives and guidelines to make their products commensurate with optimal human health. Federal regulatory agencies should assist in providing the appropriate guidelines for such actions, including labeling of these products. The Task Force believes that the widespread use of such measures may be particularly effective in reducing death and disability from arteriosclerosis.

APPENDIX A

ACKNOWLEDGMENTS

In submitting its report, the National Heart and Lung Institute Task Force on Arteriosclerosis received assistance from the panel members listed in Appendix B and from the following individuals: Dr. Hugh A. McAllister, Armed Forces Institute of Pathology; Dr. Joseph L. Goldstein, University of Washington; and Dr. David C. Jenkins, University of North Carolina.

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APPENDIX B

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APPENDIX C

GLOSSARY

ANEURYSM

A spindle-shaped or sac-like bulging of the wall of a vein or artery including the aorta, due to an abnormality present at birth or to later weakening of the wall by disease.

ANGINA PECTORIS

A condition in which the heart muscle receives an insufficient blood supply, causing distinctive pain in the chest, and often in the left arm and shoulder. It commonly results when the arteries supplying the heart muscle (coronaries) are narrowed by atherosclerosis. See Coronary Atherosclerosis.

ANGIOGRAPHY

An invasive technique for diagnosing atherosclerosis involving X-ray examination of the heart and great blood vessels to visualize the course of a fluid opaque to X-rays which has been injected into the blood stream. See Noninvasive Diagnostic Technique.

ANTICOAGULANT

A drug which delays clotting of the blood. When a blood vessel is plugged by a clot, the drug tends to prevent new clots from forming, or existing clots from enlarging, but does not dissolve an existing clot.

AORTA

The main trunk artery which conducts blood from the lower left chamber of the heart. It originates at the base of the heart, arches up over the heart like a cane handle, and passes down through the chest and abdomen in front of the spine. Lesser arteries which conduct blood to all parts of the body except the lungs branch from the aorta.

AORTOGRAPHY

X-ray examination of the aorta (main artery conducting blood from the lower left chamber of the heart to the body) and its main branches. It is made possible by the injection of a dye which is opaque to X-rays.

APHASIA

Loss or impairment of the power to express oneself by speech, writing, or signs, or to comprehend spoken or written language.

APOPLEXY

Frequently called apoplectic stroke or simply a stroke. A sudden interruption of the blood supply to a part of the brain caused by the obstruction or rupture of an artery. Initially it causes a loss of consciousness, sensation, or voluntary motion, and may leave a part of the body (frequently one side) temporarily or permanently paralyzed.

ARRHYTHMIA

An abnormal rhythm of the heart beat.

ARTERIOSCLEROSIS

Commonly called hardening of the arteries. This broad term includes a variety of conditions that cause the artery walls to become thick and hard. See Atherosclerosis

ARTERY

Blood vessels which carry blood away from the heart to the various parts of the body. They usually carry oxygenated blood; an exception is the pulmonary artery which carries unoxygenated blood from the heart to the lungs for oxygenation.

ATHEROGENESIS

The chain of events leading to the development of atheromatous lesions in the arterial wall.

ATHEROMA

A deposit of fatty (and other) substances in the inner lining of the artery wall characteristic of atherosclerosis. Plural form of the word is atheromata. See Atherosclerosis.

ATHEROSCLEROSIS

A form of arteriosclerosis in which the inner layer of the artery wall is made thick and irregular by deposits of a fatty substance. These deposits (called atheromata) project above the surface of the inner layer of the artery, and thus decrease the diameter of the internal channel of the vessel. See Arteriosclerosis.

ATROPHY

A wasting away or reduction in size of an organ or part of the body.

BLOOD PRESSURE

The pressure of the blood in the arteries.

1. Systolic blood pressure. Blood pressure when the heart muscle is contracted (systole).

2. Diastolic blood pressure. Blood pressure when the heart muscle is relaxed between beats (diastole). Blood pressure is generally expressed by two numbers, as 120/80, the first representing the systolic, and the second, the diastolic pressure.

BRUIT

A sound or murmur heard in auscultation (listening to sounds within the body, usually with a stethoscope).

CARDIAC

Pertaining to the heart.

CARDIOVASCULAR

Pertaining to the heart and blood vessels.

CARDIOVASCULAR-RENAL DISEASE

Disease involving the heart, blood vessels, and kidneys.

CEREBRAL VASCULAR ACCIDENT

Sometimes called cerebrovascular accident, apoplectic stroke, or simply stroke. A decreased blood supply to some part of the brain, generally caused by one of the following four conditions:

1. a blood clot forming in the vessel (cerebral thrombosis)
2. a rupture of the blood vessel wall (cerebral hemorrhage)
3. a piece of clot or other material from another part of the vascular system which flows to the brain or obstructs a cerebral vessel (cerebral embolism)
4. pressure on a blood vessel as by a tumor.

CEREBROVASCULAR

Pertaining to the blood vessels in the brain.

CHOLESTEROL

A fat-like substance present in the blood, the brain, and all other tissues throughout the body, as well as in much of the food we eat. Cholesterol has been implicated in the development of atherosclerosis. In blood tests, the normal level for Americans is generally assumed to be between 180 and 230 milligrams per 100 ml. The optimal blood cholesterol levels for a given age, sex, and race are not known. However, in men with levels of 220–249 mg. per 100 ml. the incidence of coronary atherosclerosis has been shown to be 48% higher than in men with cholesterols lower than 220 mg. per 100 ml.

CIRCULATORY

Pertaining to the heart, blood vessels, and the circulation of the blood.

CLAUDICATION

Pain and lameness or limping caused by defective circulation of the blood in the vessels of the limbs.

CLOSED POPULATION

A study population composed of institutionalized individuals.

COAGULATION

Process of changing from a liquid to a thickened or solid state which results in formation of a clot.

COLLATERAL CIRCULATION

Circulation of the blood through nearby smaller vessels when a main vessel has been blocked up.

CONGESTIVE HEART FAILURE

When the heart is unable adequately to pump out all the blood that returns to it, there is a backing up of blood in the veins leading to the heart. A congestion or accumulation of fluid in various parts of the body (lungs, legs, abdomen, etc.) may result from the heart's failure to maintain a satisfactory circulation. See Myocardial Insufficiency.

CONTROL GROUP

Those individuals in a study who are serving as a standard against which the experimental group can be compared.

CORONARY ARTERIES

Two arteries, arising from the beginning of the aorta, arching down over the top of the heart, and conducting blood to the heart muscle.

CORONARY ATHEROSCLEROSIS

Commonly called coronary heart disease. An irregular thickening of the inner layer of the walls of the arteries which conduct blood to the heart muscle. The internal channel of these arteries (the coronaries) becomes narrowed and the blood supply to the heart muscle is reduced. See Atherosclerosis.

CORONARY OCCLUSION

An obstruction (generally a blood clot) in a branch of one of the coronary arteries which hinders the flow of blood to some part of the heart muscle. This part of the heart muscle then dies because of lack of blood supply. Sometimes called a coronary heart attack, or simply a heart attack.

CORONARY THROMBOSIS

Formation of a clot in a branch of one of the arteries which conduct blood to the heart muscle (coronary arteries). A form of coronary occlusion. See Coronary Occlusion.

DIABETES MELLITUS

A metabolic disorder in which the ability to metabolize carbohydrates is impaired.

DIGITALIS

A drug prepared from the leaves of foxglove plant which strengthens the force of the contraction of the heart muscle, slows the rate of contraction of the heart, improves the efficiency of the heart, and promotes the elimination of excess fluid from body tissues.

DIRECT COSTS

Expenditures for hospital and nursing home care, physicians' and other medical professional services, drugs, research, and other non-personal services.

DIURETIC

A medicine which promotes the excretion of urine. Several types of drugs may be used, such as mercurials, chlorothiazide, and benzothiadiazine derivatives.

EDEMA

Swelling due to abnormally large amounts of fluid in the tissues of the body.

ELECTROCARDIOGRAM

Often referred to as EKG or ECG. A graphic record of the electric currents produced by the heart.

EMBOLISM

The blocking of a blood vessel by a clot or other substance that entered the blood stream.

EMBOLUS

A blood clot (or other substance such as air, fat, tumor) inside a blood vessel which is carried in the bloodstream to a smaller vessel where it becomes an obstruction to circulation. See Thrombus.

EPIDEMIOLOGY

The science dealing with the factors that determine the frequency and distribution of a disease in a human community.

ESSENTIAL HYPERTENSION

Sometimes called primary hypertension, and commonly known as high blood pressure. An elevated blood pressure not caused by kidney or other evident disease.

ETIOLOGY

The sum of knowledge about the causes of a disease.

EXPERIMENTAL GROUP

Those individuals in a study who are given experimental therapy or other type of intervention.

FATTY STREAK

Cells filled with lipid and located in the arterial intima. It is probably the earliest manifestation of atherosclerosis.

FIBRILLATION

Uncoordinated ineffective contractions of the heart muscle.

FIBRIN

An elastic protein which forms the essential portion of a blood clot.

FIBRINOLYTIC

Having the ability to dissolve a blood clot.

FRAMINGHAM HEART STUDY

A study of cardiovascular diseases conducted by the National Heart and Lung Institute in Framingham, Massachusetts.

GANGRENE

Death of tissues in an area of the body, as a result of loss of blood supply.

GENETICS

The study of heredity.

GLUCOSE TOLERANCE TEST

A laboratory test used in the diagnosis of diabetes mellitus. A person is given sugar in the form of glucose. At periodic intervals, the urine and the blood are examined for the amount of sugar present.

HEMIPLEGIA

Paralysis of one side of the body caused by damage to the opposite side of the brain. The paralyzed arm and leg are opposite to the side of the brain damage because the nerves cross in the brain, and one side of the brain controls the opposite side of the body. Such paralysis is sometimes caused by a blood clot or hemorrhage in a blood vessel in the brain. See Stroke.

HEMODYNAMICS

The study of the flow of blood and the forces involved.

HEMORRHAGE

Loss of blood from a blood vessel. In external hemorrhage blood escapes from the body. In internal hemorrhage blood passes into the tissues surrounding the ruptured blood vessel.

HYPERCHOLESTEROLEMIA

An excess of a fatty substance called cholesterol in the blood. See Cholesterol.

HYPERLIPEMIA

An excess of fat or lipids in the blood. Also called hyperlipidemia or hyperlipoproteinemia.

HYPERLIPOPROTEINEMIA

See Hyperlipemia.

HYPERTENSION

Commonly called high blood pressure. An unstable or persistent elevation of blood pressure above the normal range, which may eventually lead to increased heart size and kidney damage. See Primary Hypertension and Secondary Hypertension.

HYPERTROPHY

The enlargement of a tissue or organ due to increase in the size of its constituent cells. This may result from a demand for increased work.

INCIDENCE

The number of new cases of a disease developing in a given population during a specified period of time, such as a year.

INDIRECT COSTS

Lost earnings associated with man-years lost to productivity due to illness or disability.

INFARCT

An area of a tissue which is damaged or dies as a result of not receiving a sufficient blood supply. Frequently used in the phrase "myocardial infarct" referring to an area of the heart muscle damaged or killed by an insufficient flow of blood through the coronary arteries which normally supply it.

INTERVENTRICULAR SEPTUM

Sometimes called ventricular septum. Muscular wall, thinner at the top, dividing the left and right lower chambers of the heart which are called ventricles.

INTIMA

The innermost layer of a blood vessel.

IN VITRO

Literally means "in glass", hence in a laboratory vessel. Describes a phenomenon studied outside a living body under laboratory conditions. See In Vivo.

IN VIVO

In a living organism. Describes a phenomenon studied in a living body. See In Vitro.

ISCHEMIA

A local, usually temporary, deficiency of blood in some part of the body, often caused by a constriction or an obstruction in the blood vessel supplying that part.

ISOTOPE

Any of two or more forms of the same element differing in atomic weight. Some are radioactive.

LESION

An abnormality in the structure or function of a tissue or part of the body.

LIPID

Substances soluble in organic solvents but poorly, or not at all, in water.

LIPOPROTEIN

A complex of lipid and protein molecules. Lipoproteins are classified according to their density (high, low, very low) or electrical charge (alpha, beta, pre-beta).

LUMEN

The passageway inside a tubular organ. Vascular lumen is the passageway inside a blood vessel.

METABOLISM

A general term to designate all chemical changes which occur to substances within the body.

MONO-UNSATURATED FAT

A fat so constituted chemically that it is capable of combining with additional hydrogen but not as much hydrogen as a poly-unsaturated fat. These fats in the diet have little effect on the amount of cholesterol in the blood. Olive oil is rich in mono-unsaturated fat. See Poly-unsaturated Fat.

MORBIDITY RATE

The ratio of the number of cases of a disease to the number of well people in a given population during a specified period of time, such as a year. The term "morbidity" involves two separate concepts.

a. Incidence is the number of new cases of a disease developing in a given population during a specified period of time, such as a year.

b. Prevalence is the number of cases of a given disease existing in a given population at a specified moment of time.

MORBIDITY RATIO

A ratio of the observed number of cases of disease in a population of interest compared to the number of cases expected for that population.

MORTALITY RATE

The number of deaths from a specific cause that occurred in a unit of population in a specified period of time, such as a year.

MORTALITY RATIO

A ratio of the observed number of deaths in a population of interest compared to the number of deaths expected for that population.

MYOCARDIAL INFARCTION

The damaging or death of an area of the heart muscle (myocardium) resulting from a reduction in the blood supply reaching that area.

MYOCARDIAL INSUFFICIENCY

An inability of the heart muscle (myocardium) to maintain normal circulation. See Congestive Heart Failure.

MYOCARDIUM

The muscular wall of the heart. The thickest of the three layers of the heart wall, it lies between the inner layer (endocardium) and the outer layer (epicardium).

NITROGLYCERIN

A drug (one of the nitrates) which relaxes the muscles in the blood vessels and widens them (vasodilation). Often used to relieve attacks of angina pectoris and spasm of coronary arteries.

NONINVASIVE DIAGNOSTIC TECHNIQUE

Technique for diagnosing disease which does not

necessitate introducing an instrument or other device into the body. Methods for accurate non-invasive diagnosis of the degree of atherosclerosis on the inside of the wall of an artery are not yet available. See Angiography.

OPEN POPULATION

A study population composed of free-living volunteers as opposed to institutionalized individuals. See Closed Population.

PAPILLARY MUSCLES

Small bundles of muscles in the wall of the lower chambers of the heart to which the cords leading to the leaflets of the valves (chordae tendineae) are attached. When the valves are closed, these muscles contract and tighten the cords which hold the valves firmly shut.

PARAPLEGIA

Loss of motion in the legs and lower part of the body. This most commonly is due to damage to the spinal cord, but sometimes results from a clot or hemorrhage in an artery conducting blood to spinal cord.

PATHOGENESIS

The chain of events leading to the development of disease.

PATHOLOGY

The study of the essential nature of disease and the structural and functional changes it causes.

PLACEBO

A preparation containing something that can neither help nor harm the person who takes it. In testing new drugs, the experimental group is given the drug and a control group is given a placebo that looks and tastes the same.

PLAQUE

A raised cap-like lesion on the arterial intima.

PLASMA

The cell-free liquid portion of uncoagulated blood. It is different from serum which is the fluid portion of the blood obtained after coagulation.

PLETHYSMOGRAPHY

Recording of the changes in the size of an organ or limb as modified by the circulation of the blood in it.

POLY-UNSATURATED FAT

A fat so constituted chemically that it is capable of combining with additional hydrogen. These fats are usually liquid oils of vegetable origin, such as corn oil or safflower oil. A diet with a high poly-unsaturated fat content tends to lower the amount of cholesterol in the blood. See Mono-unsaturated Fat.

PREVALENCE

The number of cases of a given disease existing in a given population at a specified moment of time.

PRIMARY HYPERTENSION

Sometimes called essential hypertension, and commonly known as high blood pressure. An elevated blood pressure not caused by kidney or other evident disease.

PRIMARY PREVENTION

Measures taken so that a given disease does not occur.

PROSTHETIC BLOOD VESSEL

An artificial substitute for part or all of a given blood vessel.

PULMONARY ARTERY

The large artery which conveys poorly oxygenated (venous) blood from the lower right chamber of the heart to the lungs. This is the only artery in the body which carries unoxygenated blood.

PULMONARY CIRCULATION

The circulation of the blood through the lungs, the flow being from the right lower chamber of the heart (right ventricle) through the lungs, back to the left upper chamber of the heart (left atrium). See Systemic Circulation.

RADIOGRAPHY

The making of photographs or records on a sensitive film by projection of X-rays through a part of the body.

REHABILITATION

The return of a person disabled by accident or disease to the maximum attainable physical, mental, emotional, social, and economic usefulness, and, if employable, an opportunity for gainful employment.

RISK FACTOR

The characteristic of an individual which is associated with a greater than average incidence of a specified disease.

SATURATED FAT

A fat so constituted chemically that it is not capable of combining with any more hydrogen. These are usually the solid fats of animal origin such as the fats in milk, butter, meat, etc. A diet high in saturated fat tends to increase the amount of cholesterol in the blood.

SCLEROSIS

Hardening, usually due to an accumulation of fibrous tissue.

SECONDARY HYPERTENSION

An elevated blood pressure caused by (i.e., secondary to) certain specific diseases.

SECONDARY PREVENTION

Measures taken to prevent recurrence of disease.

SERUM

The fluid portion of blood that remains after the cellular elements have been removed by coagulation. It is different from plasma which is the cell-free liquid of uncoagulated blood.

SHOCK

The signs and symptoms associated with failure or collapse of the circulatory system. The signs of shock include weakness, extreme pallor, cold and moist skin, weak and rapid pulse, irregular and shallow breathing, thirst, nausea, scanty secretion of urine, and low blood pressure.

SODIUM

A mineral essential to life, found in nearly all plant and animal tissue. Table salt (sodium chloride) is nearly half sodium. In some types of heart disease the body retains an excess of sodium and water, and, therefore, treatment includes restriction of sodium intake.

STROKE

Also called apoplectic stroke. See Cerebrovascular Accident.

SYNDROME

A set of symptoms that occur together and are therefore given a name to indicate that particular combination.

SYSTEMIC CIRCULATION

The circulation of the blood through all parts of the body except the lungs, the flow being from the left lower chamber of the heart (left ventricle) through the body, back to the right upper chamber of the heart (right atrium). See Pulmonary Circulation.

THROMBOLYTIC AGENTS

Substances that dissolve blood clots.

THROMBOSIS

The formation or presence of a blood clot (thrombus) inside a blood vessel or cavity of the heart.

THROMBUS

A blood clot that forms inside a blood vessel or cavity of the heart. See Embolus.

UNSATURATED FAT

A term used loosely in popular writing and advertising. It usually includes both mono-unsaturated and poly-unsaturated fats.

UROGRAPHY

Radiography of the urinary tract.

VEIN

Any one of a series of vessels of the vascular system which carries blood from various parts of the body back to the heart. All veins in the body conduct unoxygenated blood except the pulmonary veins which conduct freshly oxygenated blood from the lungs back to the heart.

VENTRICLE

One of the two lower chambers of the heart. Left ventricle pumps oxygenated blood through the arteries to the body. Right ventricle pumps unoxygenated blood through the pulmonary artery to the lungs.

VERTIGO

A sensation that the external world is revolving around the patient.

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